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1: Biotechnology (N Y). 1992 Oct;10(10):1121-7.

High level expression on a chimeric anti-ganglioside GD2 antibody: genomic kappa sequences improve expression in COS and CHO cells.

Fouser LA, Swanberg SL, Lin BY, Benedict M, Kelleher K, Cumming DA, Riedel GE.

Genetics Institute, Cambridge, Massachusetts 02140.

We report a flexible strategy for the high level expression of a recombinant human monoclonal antibody (mAb) in Chinese hamster ovary (CHO) cells, initially using COS monkey kidney cell transfections to evaluate rapidly modifications to immunoglobulin (Ig) DNA constructs. Using sequential transfections with two amplifiable markers, we generated CHO cell lines and clones that secrete 80-110 micrograms/10(6) cells/24 hours of a mouse-human chimeric IgG1 kappa mAb. This cellular productivity is considerably greater than most murine hybridomas and transfected myelomas. Our data also demonstrate that genomic kappa sequences can improve mAb expression in COS and CHO cells. As a paradigm, we focused our expression studies on a human chimeric form of 3F8, a murine mAb that binds to ganglioside GD2 on neuroblastoma and melanoma tumor cells.

PMID: 1382457 [PubMed - indexed for MEDLINE]

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cells in mice. [Mol Immunol.

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Characterization of huma
IgG1 monoclonal antibod
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against gangliosides expressed on human cells.
Production and characterization of a set of mouse-human chimeric immunoglobulin G (IgG) subclass and IgA monoclonal antibodies with identical variable regions specific for Pseudomonas aeruginosa serotype O6 lipopolysaccharide.
Recombinant antibodies against ganglioside expressed on tumor cells.

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#31	Search **#12 and hybrid cell** Limits: **Publication Date to 1996/10/10**	17:50:52	2
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#9	Search **#1 and #8** Limits: **Publication Date to 1996/10/10**	16:45:35	19
#8	Search **two expression vectors** Limits: **Publication Date to 1996/10/10**	16:45:25	3133
#3	Search **#1 and #2** Limits: **Publication Date to 1996/10/10**	16:43:05	7
#2	Search **two vector system** Limits: **Publication Date to 1996/10/10**	16:42:54	1177
#1	Search **antibody production** Limits: **Publication Date to 1996/10/10**	16:42:39	49986

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MECHANISM OF ACTION - Immunotherapy.
USE - The antibody, its specified portion and variant are useful for treating an immune disease or disorder, e.g. rheumatoid arthritis/seronegative arthropathies, osteoarthritis, or inflammatory bowel disease. (claimed).
Dwg.0/10

L22 ANSWER 9 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-247727 [23] WPIDS
CROSS REFERENCE: 2004-247726 [23]
DOC. NO. CPI: C2004-096685
TITLE: Producing a multi-component **protein**, useful for gene expression or **cell** fusion techniques, comprises fusing recombinant **cells** containing expression cassettes encoding the components of a multimeric **protein**.
DERWENT CLASS: B04 D16
INVENTOR(S): BABCOOK, J; RYLL, T; ZENG, W
PATENT ASSIGNEE(S): (BABC-I) BABCOOK J; (RYLL-I) RYLL T; (ZENG-I) ZENG W; (ABGE-N) ABGENIX INC
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004053363	A1	20040318	(200423)*		22
WO 2004027043	A2	20040401	(200431)	EN	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003298992	A1	20040408	(200462)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004053363	A1 Cont of	US 2002-247466	20020918
		US 2003-353844	20030128
WO 2004027043	A2	WO 2003-US29869	20030917
AU 2003298992	A1	AU 2003-298992	20030917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003298992	A1 Based on	WO 2004027043

PRIORITY APPLN. INFO: US 2002-247466 20020918; US 2003-353844 20030128
AN 2004-247727 [23] WPIDS
CR 2004-247726 [23]
AB US2004053363 A UPAB: 20040928
NOVELTY - Producing a multi-component **protein** comprises fusing first and a second recombinant **cells** which contain

first and a second expression cassettes containing an amplifiable marker and encoding first and second components of the multimeric **protein** to produce a hybrid **cell** expressing the multimeric **protein**.

DETAILED DESCRIPTION - The method comprises:

(a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a first component of the multi-component **protein**, the first amplifiable marker is amplifiable by an amplification agent, where the introduction of the **polypeptide** produces a first recombinant **cell**;

(b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a second component of the multi-component **protein**, the second amplifiable marker is amplifiable by a second amplification agent, where the introduction of the **polypeptide** produces a second recombinant **cell**;

(c) optionally, repeating (b) for each remaining component of the multi-component **protein**;

(d) fusing **cells** produced from (a)-(c) to form a hybrid **cell**, which expresses the multi-component **protein**; and

(e) culturing the hybrid **cell** in the presence of the amplification agents for the first and second amplifiable markers, where the first and second recombinant not cultured in the presence of the amplification agents sufficient to provide for amplification of the amplifiable marker until after the fusing.

An INDEPENDENT CLAIM is also included for a method for **producing** an **antibody**.

USE - The method is useful for producing a multi-component **protein**. The method is useful in gene expression and **cell** fusion techniques.

ADVANTAGE - Amplification of the hybrid, fused **cells** is relatively easier, less time and resource consuming and more efficient than separate amplification of each of the parenteral recombinant **heavy chain** expressing and recombinant **light chain** expressing **cells** prior to fusion. The method also generates a **cell**, which **produces** an **antibody** at a high rate through the fusion of two kinds of **cells**, which are selected prior to fusion for high **production** of the desired heavy or **light chains**.

Dwg.0/7

L22 ANSWER 10 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-247726 [23] WPIDS
CROSS REFERENCE: 2004-247727 [23]
DOC. NO. CPI: C2004-096684
TITLE: **Producing** a multi-component **protein**, i.e. an **antibody**, for treating cancer or infections, comprises fusing mammalian **cells** containing polynucleotides encoding components of the **protein** to form a hybrid **cell** expressing the **protein**.
DERWENT CLASS: B04 D16
INVENTOR(S): BABCOOK, J; RYLL, T; ZENG, W
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (BABC-I) BABCOOK J; (RYLL-I) RYLL T; (ZENG-I) ZENG W

COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004053359	A1	20040318	(200423)*		22
AU 2003298992	A1	20040408	(200462)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2004053359	A1	US 2002-247466	20020918
AU 2003298992	A1	AU 2003-298992	20030917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003298992	A1 Based on	WO 2004027043

PRIORITY APPLN. INFO: US 2002-247466 20020918; US 2003-353844 20030128
AN 2004-247726 [23] WPIDS
CR 2004-247727 [23]
AB US2004053359 A UPAB: 20040928
NOVELTY - Producing a multi-component **protein** comprises fusing mammalian **cells** containing polynucleotides encoding components of the multi-component **protein** to form a hybrid **cell** expressing the multi-component **protein**, and culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers of the polynucleotides.

DETAILED DESCRIPTION - The method above comprises:

(a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a first component of the multi-component **protein**, where the first amplifiable marker is amplifiable by an amplification agent;

(b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a second component of the multi-component **protein**, where the second amplifiable marker is amplifiable by the same amplification agent as the first amplifiable marker;

(c) optionally, repeating step (B) for each remaining component of the multi-component **protein**;

(d) fusing **cells** produced from (A)-(C) to form a hybrid **cell**, which expresses the multi-component **protein**; and

(e) culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers.

An INDEPENDENT CLAIM is also included for a method for **producing** an **antibody** comprising fusing a first recombinant mammalian **cell** and a second recombinant mammalian **cell** to form a hybrid **cell**, where the first **cell** contains a first polynucleotide comprising a first amplifiable marker and a sequence encoding a **heavy chain polypeptide**, and where the second **cell**

contains a second polynucleotide comprising a second amplifiable marker and a sequence encoding a **light chain polypeptide**, where the first and second amplifiable markers are amplifiable by the same amplification agent, and culturing the hybrid **cell** in the presence of the amplification agent for the first and second amplifiable markers.

ACTIVITY - Cytostatic; Antibacterial; Immunomodulatory. No biological data given.

MECHANISM OF ACTION - None given.

USE - The methods, polynucleotides, mammalian **cells** and amplifiable markers are useful for **producing** a multimeric **protein**, i.e. an **antibody**, used as therapeutic agents for human disease, such as cancer, microbial infections or disorders of the immune system.

ADVANTAGE - Unlike prior art, the present method generates a **cell** which **produces** an **antibody** at a high rate. Amplification of the hybrid, fused **cell** is relatively easier, less time and resource consuming, and more efficient than separate amplification of each of the parental recombinant **heavy chain**-expressing **cell** and recombinant **light chain**-expressing **cell** prior to fusion.

Dwg.0/7

L22 ANSWER 11 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-616322 [60] WPIDS
DOC. NO. CPI: C2004-222064
TITLE: **Producing** a **protein** e.g. a human **antibody**, comprises culturing mammalian **cells** introduced separately with polynucleotides encoding **antibody** heavy and **light chains** and fusing cultured **cells** to form a hybrid **cell** expressing **antibody**.
DERWENT CLASS: B04 D16
INVENTOR(S): DAVIS, C G; GREEN, L; HORI, N; JAKOBOVITS, A; WEBER, R F; ZSEBO, K M
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (NISB) JAPAN TOBACCO INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 2004200848	A1	20040325	(200460)*		45

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
AU 2004200848	A1	AU 2004-200848	20040303

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004200848	A1 Div ex	AU 768101

PRIORITY APPLN. INFO: AU 2004-200848 20040303
AN 2004-616322 [60] WPIDS

AB AU2004200848 A UPAB: 20040920
NOVELTY - **Producing** (M1) an **antibody**, comprises introducing a polynucleotide encoding a **heavy chain polypeptide** of an **antibody** into a mammalian **cell**, introducing a second polynucleotide encoding a **light chain polypeptide** of the **antibody** into a second mammalian **cell**, culturing each of the **cells** separately and fusing the **produced** cultured **cells** to form a hybrid **cell** expressing **antibody**.
DETAILED DESCRIPTION - **Producing** (M1) an **antibody**, involves (a) introducing a first polynucleotide into a first mammalian **cell**, where the first polynucleotide comprises a first amplifiable marker and a sequence encoding a **heavy chain polypeptide** of an **antibody**, (b) introducing a second polynucleotide into a second mammalian **cell**, where the second polynucleotide comprises a second amplifiable marker and a sequence encoding a **light chain polypeptide** of the **antibody**, (c) culturing each of the first and second **cells** separately in the presence of an amplification agent, where the first and second amplifiable markers are amplified by the same amplification agent, and (d) fusing the cultured **cells produced** by steps (a)-(c) to form a hybrid **cell**, where the hybrid **cells** express the **antibody**. (M1) optionally involves culturing a first recombinant mammalian **cell** in the presence of a first amplification agent to **produce** a first amplified recombinant **cell**, where the first **cell** comprises a first polynucleotide comprising a first amplifiable marker and a sequence encoding a **heavy chain polypeptide**, culturing a second recombinant mammalian **cell** in the presence of a second amplification agent to **produce** a second amplified recombinant **cell**, where the second **cell** comprises a second polynucleotide comprising a second amplifiable marker and a sequence encoding a **light chain polypeptide**, where the first and second amplifiable markers are amplified by the same amplification agent, and fusing the first and second amplified recombinant mammalian **cells** to form a hybrid **cell**, where the hybrid **cell** expressed an **antibody**.
USE - (M1) is useful for **producing** a human **antibody** (claimed).
ADVANTAGE - In (M1), the first **cell** expressing desired **heavy chain** and second **cell** expressing desired **light chain** are selected for one or more desirable characteristics such as high production rate of the heavy or **light chain**, prior to the fusion (claimed).
Dwg.0/10

L22 ANSWER 12 OF 24 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004544758 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15459912
TITLE: Comparative proteomic analysis of **GS**-NS0 murine myeloma **cell** lines with varying recombinant monoclonal **antibody production** rate.
AUTHOR: Smales C M; Dinnis D M; Stansfield S H; Alete D; Sage E A; Birch J R; Racher A J; Marshall C T; James D C
CORPORATE SOURCE: Research School of Biosciences, University of Kent,

Canterbury, Kent, CT2 7NJ, United Kingdom.
SOURCE: Biotechnology and bioengineering, (2004 Nov 20) 88 (4) 474-88.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041102
Last Updated on STN: 20050422
Entered Medline: 20050421

AB We have employed an inverse engineering strategy based on quantitative proteome analysis to identify changes in intracellular **protein** abundance that correlate with increased specific recombinant monoclonal **antibody production** (qMab) by engineered murine myeloma (NS0) **cells**. Four homogeneous NS0 **cell** lines differing in qMab were isolated from a pool of primary transfectants. The proteome of each stably transfected **cell** line was analyzed at mid-exponential growth phase by two-dimensional gel electrophoresis (2D-PAGE) and individual **protein** spot volume data derived from digitized gel images were compared statistically. To identify changes in **protein** abundance associated with qMab datasets were screened for **proteins** that exhibited either a linear correlation with **cell** line qMab or a conserved change in abundance specific only to the **cell** line with highest qMab. Several **proteins** with altered abundance were identified by mass spectrometry. **Proteins** exhibiting a significant increase in abundance with increasing qMab included molecular chaperones known to interact directly with nascent immunoglobulins during their folding and assembly (e.g., BiP, endoplasmin, **protein** disulfide isomerase). 2D-PAGE analysis showed that in all **cell** lines Mab **light chain** was more abundant than **heavy chain**, indicating that this is a likely prerequisite for efficient Mab production. In summary, these data reveal both the adaptive responses and molecular mechanisms enabling mammalian **cells** in culture to achieve high-level recombinant monoclonal **antibody production**.

L22 ANSWER 13 OF 24 WPIDS
ACCESSION NUMBER: 2003-679629 [64] WPIDS
CROSS REFERENCE: 2003-679625 [64]
DOC. NO. CPI: C2003-185720
TITLE: New nucleic acid, useful for **producing** humanized or chimeric **antibodies**, or fusion **proteins** comprising the **antibodies**, which are G250-specific and useful for treating inflammatory conditions, e.g. rheumatoid arthritis or asthma.
DERWENT CLASS: B04 D16
INVENTOR(S): RENNER, C; SCOTT, A
PATENT ASSIGNEE(S): (LUDW-N) LUDWIG INST CANCER RES
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2003068924 A2 20030821 (200364)* EN 80
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003215188 A1 20030904 (200428)
EP 1507859 A2 20050223 (200515) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003068924	A2	WO 2003-US4243	20030212
AU 2003215188	A1	AU 2003-215188	20030212
EP 1507859	A2	EP 2003-711002	20030212
		WO 2003-US4243	20030212

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003215188	A1 Based on	WO 2003068924
EP 1507859	A2 Based on	WO 2003068924

PRIORITY APPLN. INFO: US 2002-355838P 20020213
AN 2003-679629 [64] WPIDS
CR 2003-679625 [64]
AB WO2003068924 A UPAB: 20050303
NOVELTY - An isolated nucleic acid molecule, which encodes a fusion **protein** comprising a chimerized antibody molecule, and a tumor necrosis factor molecule or its fragment, is new. The antibody specifically binds to a target. The fragment of the tumor necrosis factor molecule possesses the **cell** killing properties of a full-length tumor necrosis factor molecule.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a chimeric fusion **protein** encoded by the isolated nucleic acid molecule;

(2) an expression vector comprising the isolated nucleic acid molecule operably linked to a promoter; and

(3) a recombinant **cell** comprising the isolated nucleic acid molecule or the expression vector.

ACTIVITY - Antiinflammatory; Antirheumatic; Antiarthritic; Antipsoriatic; Antiasthmatic; Neuroprotective; Virucide; Antibacterial; Immunosuppressive; Nephrotropic; Antiarteriosclerotic. No biological data given.

MECHANISM OF ACTION - GM-CSF-Antagonist; CD30-Antagonist; G250 Antagonist.

USE - The nucleic acid is useful for the expression of **proteins**, especially **antibodies**, as well as fusion **proteins** that incorporate the **antibody** and a **protein**. The expression vector is useful in **manufacturing** a recombinant **antibody** (e.g. a fully human, humanized or chimeric **antibody**) in a eukaryotic

cell (claimed). The **antibody** is useful in therapy, particularly for targeting G250 and blocking granulocyte-macrophage stimulating factor (GM-CSF), which is involved in the development of rheumatoid arthritis. The **antibody** is useful for treating inflammatory conditions, e.g. psoriasis, asthma, inflammatory bowel disease, multiple sclerosis, viral or bacterial pneumonia, septic shock, nephritis, or arteriosclerosis.
Dwg.0/5

L22 ANSWER 14 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-430422 [40] WPIDS
DOC. NO. CPI: C2003-113847
TITLE: New nucleic acid molecule useful for producing a heteromeric complex comprises a first nucleic acid operably linked to a second nucleic acid encoding a subunit of a selectable marker .
DERWENT CLASS: B04 D16
INVENTOR(S): BIANCHI, A A; MCGREW, J T
PATENT ASSIGNEE(S): (BIAN-I) BIANCHI A A; (MCGR-I) MCGREW J T; (IMMV) IMMUNEX CORP
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003035887	A1	20030501	(200340)*	EN	28
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2003082735	A1	20030501	(200340)		
EP 1434871	A1	20040707	(200444)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
AU 2002331883	A1	20030506	(200461)		
JP 2005511031	W	20050428	(200530)		20
MX 2004002489	A1	20050101	(200564)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003035887	A1	WO 2002-US29985	20020920
US 2003082735	A1 Provisional	US 2001-323954P	20010920
		US 2002-251447	20020920
EP 1434871	A1	EP 2002-768877	20020920
		WO 2002-US29985	20020920
AU 2002331883	A1	AU 2002-331883	20020920
JP 2005511031	W	WO 2002-US29985	20020920
		JP 2003-538387	20020920
MX 2004002489	A1	WO 2002-US29985	20020920
		MX 2004-2489	20040316

FILING DETAILS:

PATENT NO	KIND	PATENT NO

EP 1434871	A1	Based on	WO 2003035887
AU 2002331883	A1	Based on	WO 2003035887
JP 2005511031	W	Based on	WO 2003035887
MX 2004002489	A1	Based on	WO 2003035887

PRIORITY APPLN. INFO: US 2001-323954P 20010920; US 2002-251447 20020920

AN 2003-430422 [40] WPIDS

AB WO2003035887 A UPAB: 20030624

NOVELTY - A new isolated nucleic acid molecule comprises a first nucleic acid encoding a **polypeptide**, where the first nucleic acid is operably linked to a second nucleic acid encoding a subunit of a selectable marker. The subunit is capable of interacting with a different subunit of the selectable marker for providing a selectable activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant vector comprising the isolated nucleic acid molecule;

(2) a host **cell** that has been genetically engineered to contain the isolated nucleic acid molecule; and

(3) producing a heteromeric complex.

USE - The nucleic acid is useful for producing a heteromeric complex (claimed).

ADVANTAGE - The invention decreases the time required to select for **cells** expressing high levels of a desired recombinant heteromeric **polypeptide** complex.

Dwg.0/0

L22 ANSWER 15 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-128758 [13] WPIDS

DOC. NO. CPI: C2004-051462

TITLE: New bicistronic expression vector for animal **cells**, a transformed **cell** line containing the vector and a method for **producing antibody proteins** using them.

DERWENT CLASS: B04 C06 D16

INVENTOR(S): JANG, H S; JUNG, J G; PARK, U Y; RA, G B; SIM, D S; YANG, J Y; YOO, J S; YOON, H S; CHANG, H S; CHUNG, J G; PARK, W Y; RAH, G B; SHIM, D S

PATENT ASSIGNEE(S): (GLDS) LG LIFE SCI LTD

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
KR 2003062118	A	20030723	(200413)*		1
KR 450266	B	20040930	(200510)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
KR 2003062118	A	KR 2002-2544	20020116
KR 450266	B	KR 2002-2544	20020116

FILING DETAILS:

PATENT NO	KIND		PATENT NO
KR 450266	B	Previous Publ.	KR 2003062118

PRIORITY APPLN. INFO: KR 2002-2544 20020116
AN 2004-128758 [13] WPIDS
AB KR2003062118 A UPAB: 20040223
NOVELTY - A bicistronic expression vector for animal **cells**, a transformed **cell** line containing the same vector and a method for **producing antibody proteins** using the same are provided, effectively expressing various genes such as an antigen gene.

DETAILED DESCRIPTION - A bicistronic expression vector for animal **cells** comprises a cytomegalovirus(CMV) promoter required for **producing** the transcriptional RNA, a foreign gene selected from **light chain** gene or **heavy chain** gene of an **antibody**, an IRES sequence, a selective gene and a poly(A) sequence, sequentially, wherein the selective gene is dihydroxyfolate reductase(**DHFR**) or neomycin resistance gene(NEOR); the bicistronic expression vector is selected from pLCM-MoK(KCTC 10151BP), pLCD-MoK(KCTC 10151BP), pLCN-MoH(KCTC 10150BP) and pANTIBODY(KCTC 10152BP). A transformed animal **cell** is **produced** by transformation with the bicistronic expression vector. A method for **producing** the foreign gene selected from the **light chain** or **heavy chain** of the **antibody** is characterized by culturing the transformed animal **cell**.
Dwg.1/10

L22 ANSWER 16 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003041514 EMBASE
TITLE: Thyroid-stimulating monoclonal antibodies.
AUTHOR: Sanders J.; Jeffreys J.; Depraetere H.; Richards T.; Evans M.; Kiddie A.; Brereton K.; Groenen M.; Oda Y.; Furmaniak J.; Rees Smith B.
CORPORATE SOURCE: Dr. B. Rees Smith, FIRS Laboratories, RSR Ltd., Parc Ty Glas, Llanishen, Cardiff, CF14 5DU, United Kingdom
SOURCE: Thyroid, (1 Dec 2002) Vol. 12, No. 12, pp. 1043-1050.
Refs: 44
ISSN: 1050-7256 CODEN: THYRER
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030207
Last Updated on STN: 20030207
AB Thyrotropin (TSH) receptor monoclonal antibodies (TSHR mAbs) were obtained from cDNA-immunized NMRI mice. Three mAb immunoglobulin **Gs** (IgGs) (TSmAbs 1-3) that had distinct V(H) and V(L) region sequences stimulated cyclic adenosine monophosphate (cAMP) production in isolated porcine thyroid **cells** greater than 10x basal and as little as 20 ng/mL (0.13 nmol/L) of TSmAb 1 IgG caused a 2x basal stimulation. TSmAb 1 and 2 Fab fragments were also effective stimulators and thyroid-stimulating activities of the IgGs and Fabs were confirmed using TSHR transfected Chinese hamster ovary (CHO)

cells. The TSmAbs also inhibited (125)I-labeled TSH binding to TSHR-coated tubes by 50% or more at concentrations of 1 μg/mL or less and gave 15%-20% inhibition at 20-50 ng/mL. (125)I-labeled TSmAbs bound to TSHR-coated tubes with high affinity (.apprx.10(10) L/mol) and this binding was inhibited by TSHR autoantibodies with both TSH agonist and antagonist activities. Inhibition of labeled TSmAb binding by Graves' sera correlated well with inhibition of TSH binding ($r = 0.96$; $n = 18$; $p < 0.001$ for TSmAb 2). The TSmAbs have considerable potential as (1) new probes for TSHR structure-function studies, (2) reagents for new assays for TSHR autoantibodies, and (3) alternatives to recombinant TSH in various in vivo applications.

L22 ANSWER 17 OF 24 MEDLINE on STN
ACCESSION NUMBER: 2000418704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10941907
TITLE: Single-chain antibodies against human insulin-like growth factor I receptor: expression, purification, and effect on tumor growth.
AUTHOR: Li S L; Liang S J; Guo N; Wu A M; Fujita-Yamaguchi Y
CORPORATE SOURCE: Department of Molecular Biology, Beckman Research Institute of the City of Hope, Duarte, CA 91010, USA.
CONTRACT NUMBER: CA65767 (NCI)
SOURCE: Cancer immunology, immunotherapy : CII, (2000 Jul) 49 (4-5) 243-52.
Journal code: 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000905

AB Insulin-like growth factors (IGF) I and II are potent mitogens for a variety of cancer **cells**. The proliferative and anti-apoptotic actions of IGF are mediated by the IGF-I receptor (IGF-IR), to which both IGF-I and IGF-II bind with high affinity. To investigate the mitogenic and anti-apoptotic activities of IGF-IR and to achieve better inhibition of IGF-IR function, single-chain antibodies against human IGF-IR (alphaIGF-IR scFvs) were constructed and expressed. IgG cDNA encoding variable regions of light and **heavy chains** (VL and VH) from mouse IgG were cloned from a hybridoma **producing** the 1H7 alphaIGF-IR monoclonal **antibody** [Li et al., Biochem Biophys Res Commun 196: 92-98 (1993)]. The splice-overlap extension polymerase chain reaction was used to assemble a gene encoding the alphaIGF-IR scFv, including the N-terminal signal **peptide**, VL, linker **peptide**, VH, and C-terminal DYKD tag. Two types of soluble alphaIGF-IR scFvs, a prototype alphaIGF-IR scFv and its alternative type alphaIGF-IR scFv-Fc, were constructed and expressed in murine myeloma **cells**. alphaIGF-IR scFv-Fc, containing the human IgG1 Fc domain, was stably expressed in NS0 myeloma **cells**, using a **glutamine synthase** selection system, and purified from the conditioned medium of stable clones by **protein** -A--agarose chromatography. Levels of alphaIGF-IR scFv-Fc expression ranged from 40 mg/l to 100 mg/l conditioned medium. Sodium dodecyl sulfate/polyacrylamide gel electrophoresis analysis under reducing and nonreducing conditions indicated that alphaIGF-IR scFv-Fc is a dimeric antibody. alphaIGF-IR scFv-Fc retained general characteristics of the

parental 1H7 monoclonal antibody except that its binding affinity for IGF-IR was estimated to be approximately 10(8) M(-1), which was one-order of magnitude lower than that of 1H7 monoclonal antibody. Injection of alphaIGF-IR scFv-Fc (500 microg/mouse, twice a week) significantly suppressed MCF-7 tumor growth in athymic mice. These results suggest that the alphaIGF-IR scFv-Fc is a first-generation recombinant alphaIGF-IR for the potential development of future alphaIGF-IR therapeutics.

L22 ANSWER 18 OF 24 MEDLINE on STN
ACCESSION NUMBER: 1999345930 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10417224
TITLE: Cytogenetic analysis of chimeric **antibody-producing** CHO **cells** in the course of **dihydrofolate reductase**-mediated gene amplification and their stability in the absence of selective pressure.
AUTHOR: Kim S J; Lee G M
CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology 373-1, Kusong-Dong, Yusong-Gu, Taejon 305-701, Korea.
SOURCE: Biotechnology and bioengineering, (1999 Sep 20) 64 (6) 741-9.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990928

AB Previously, the highest **producing** (HP) recombinant CHO subclones isolated at various methotrexate (MTX) levels showed different **antibody production** stability during long-term culture, although they were clonally derived from CS13 transformant. In this study, genetic basis for their difference in **antibody production** stability was investigated using southern blot hybridization and fluorescence in situ hybridization (FISH) techniques. Southern analysis of HP subclones revealed that **light-chain** (**LC**) and **heavy-chain** (**HC**) cDNAs were located closely within 23 kb on an amplification unit, and the configuration of **LC** and **HC** cDNAs within this amplification unit was not disrupted during long-term culture in the absence of MTX. However, when **LC** and **HC** genes were localized on the metaphase chromosomes of HP subclones using FISH, the amplified sequences were present as an extended array on diverse marker chromosomes. HP subclones selected at higher MTX level had more kinds of marker chromosomes. CS13*-002 isolated at 0.02 microM MTX had only one marker chromosome (m002), whereas CS13*-1.0 isolated at 1 microM MTX had five different ones (m10A, m10B, m10C, m10D, and m10E). Each marker chromosome showed different fate during long-term culture of HP subclones in the absence of MTX, resulting in different degrees of stability among the HP subclones. The m10A and m10B remained unchanged, whereas the others disappeared or evolved to variants with shortened amplified arrays. The **cells** containing stable marker chromosomes constituted dominant subpopulations in CS13*-1.0, and thereby CS13*-1.0 became most stable in regard to **antibody**

production during long-term culture. Furthermore, our dual-color FISH showed that the telomeric ends of amplified arrays on the stable marker chromosomes were always surrounded by (TTAGGG)(n) sequences, indicating that (TTAGGG)(n) sequences are closely related to the stability and evolution of amplified sequences. Taken together, our data show that the assessment of genotypic stability of amplified CHO **cells** is a prerequisite for understanding their production stability during long-term culture in the absence of selection pressure.

L22 ANSWER 19 OF 24 MEDLINE on STN
ACCESSION NUMBER: 1999290079 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10361728
TITLE: Changes during subclone development and ageing of human **antibody-producing** recombinant CHO **cells**.
AUTHOR: Strutzenberger K; Borth N; Kunert R; Steinfellner W; Katinger H
CORPORATE SOURCE: Institute for Applied Microbiology, University of Agriculture, Vienna, Austria.
SOURCE: Journal of biotechnology, (1999 Apr 15) 69 (2-3) 215-26.
Journal code: 8411927. ISSN: 0168-1656.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990719

AB Some of the problems encountered with human or human-mouse heterohybridomas, such as low growth rates and high serum requirements, have led to the increased use of recombinant **cell** lines for **production** of human **antibodies**. To evaluate the suitability of such alternative **cell** lines for the **production** of human **antibodies** we have analysed several subclones with differing specific **production** rates of a recombinant CHO **cell** line. Gene copy number and site of chromosomal integration for the light and **heavy chain** and the **dhfr** gene were determined by in-situ hybridisation. Specific mRNA content was analysed by Northern blot. In addition the intracellular content in light and **heavy chain** was measured by flow cytometry and the specific secretion rates were determined. The stability of gene expression was followed in the highest producing subclone for over a year. As previously seen in heterohybridoma **cells** a high expression rate of **light chain** is beneficial in speeding up secretion rates of whole antibody. When grown in the presence of G418 and methotrexate the amplified gene copies in the genome of recombinant CHO **cells** were stable over more than 100 passages. However, the expression of **light chain**, and with it the secretion rate, decreased with time. The low intracellular concentration of **light chain** resulted in accumulation of **heavy chain** in the endoplasmic reticulum due to retention by chaperones. The specific secretion rate decreased by 50% after 100 passages. When no G418 or methotrexate were present 75% of the gene copies were lost after 100

passages.

L22 ANSWER 20 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1998-251296 [22] WPIDS
DOC. NO. CPI: C1998-078411
TITLE: **Production** of multi-component **proteins**, particularly **antibodies** - by fusing **cells** which contain nucleotide sequences encoding each of the components of the multi-component **protein**.
DERWENT CLASS: B04 D16
INVENTOR(S): DAVIS, C G; GREEN, L; HORI, N; JAKOBOVITS, A; WEBER, R F; ZSEBO, K M
PATENT ASSIGNEE(S): (ABGE-N) ABGENIX INC; (NISB) JAPAN TOBACCO INC; (ABGE-N) AVGENIX INC; (DAVI-I) DAVIS C G; (HORI-I) HORI N; (JAKO-I) JAKOBOVITS A; (ZSEB-I) ZSEBO K M
COUNTRY COUNT: 80
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9816654	A1	19980423	(199822)*	EN	44
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9749898	A	19980511	(199837)		
US 5916771	A	19990629	(199932)		
EP 931162	A1	19990728	(199934)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
KR 2000049053	A	20000725	(200116)		
US 6207418	B1	20010327	(200119)		
JP 2001505049	W	20010417	(200128)		48
AU 734800	B	20010621	(200141)		
AU 2001072174	A	20011220	(200208)#		
US 2002076763	A1	20020620	(200244)		
US 6420140	B1	20020716	(200254)		
US 2002098551	A1	20020725	(200256)#		
US 2003022291	A1	20030130	(200311)		
AU 768101	B	20031204	(200382)#		
US 6677138	B2	20040113	(200405)		
KR 416680	B	20040131	(200428)		
US 2004142430	A1	20040722	(200449)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9816654	A1		WO 1997-US18910	19971010
AU 9749898	A		AU 1997-49898	19971010
US 5916771	A		US 1996-730639	19961011
EP 931162	A1		EP 1997-912801	19971010
			WO 1997-US18910	19971010
KR 2000049053	A		WO 1997-US18910	19971010
			KR 1999-703123	19990410
US 6207418	B1	Cont of	US 1996-730639	19961011
			US 1999-342301	19990629

Searcher : Shears 571-272-2528

JP 2001505049	W		WO 1997-US18910	19971010
			JP 1998-518642	19971010
AU 734800	B		AU 1997-49898	19971010
AU 2001072174	A	Div ex	AU 1997-49898	19971010
			AU 2001-72174	20010918
US 2002076763	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
			US 2001-945387	20010830
US 6420140	B1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
			US 2001-769070	20010124
US 2002098551	A1		US 2001-769070	20010124
US 2003022291	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
		Cont of	US 2001-945387	20010830
			US 2002-155839	20020524
AU 768101	B	Div ex	AU 1997-49898	19971010
			AU 2001-72174	20010918
US 6677138	B2	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
			US 2001-945387	20010830
KR 416680	B		WO 1997-US18910	19971010
			KR 1999-703123	19990410
US 2004142430	A1	Cont of	US 1996-730639	19961011
		Cont of	US 1999-342301	19990629
		Cont of	US 2001-769070	20010124
		Cont of	US 2001-945387	20010830
			US 2003-719006	20031120

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9749898	A	Based on	WO 9816654
EP 931162	A1	Based on	WO 9816654
KR 2000049053	A	Based on	WO 9816654
US 6207418	B1	Cont of	US 5916771
JP 2001505049	W	Based on	WO 9816654
AU 734800	B	Previous Publ.	AU 9749898
		Based on	WO 9816654
AU 2001072174	A	Div ex	AU 734800
US 6420140	B1	Cont of	US 5916771
		Cont of	US 6207418
US 2003022291	A1	Cont of	US 5916771
		Cont of	US 6207418
		Cont of	US 6420140
AU 768101	B	Previous Publ.	AU 2001072174
		Div ex	AU 734800
US 6677138	B2	Cont of	US 5916771
		Cont of	US 6207418
		Cont of	US 6420140
KR 416680	B	Previous Publ.	KR 2000049053
		Based on	WO 9816654
US 2004142430	A1	Cont of	US 5916771
		Cont of	US 6207418
		Cont of	US 6420140

Searcher : Shears 571-272-2528

Cont of US 6677138

PRIORITY APPLN. INFO: US 1996-730639 19961011; US
1999-342301 19990629; AU
2001-72174 20010918; US
2001-769070 20010124; US
2001-945387 20010830; US
2002-155839 20020524; US
2003-719006 20031120

AN 1998-251296 [22] WPIDS

AB WO 9816654 A UPAB: 19980604

A method (A) for **producing** a multi-component **protein** (MCP) comprises: (a) introducing a first nucleotide sequence (NS) into a first **cell**, where the first NS encodes a first component of the MCP; (b) introducing a second NS into a second **cell**, where the second NS encodes a second component of the MCP; (c) optionally repeating step (b) for each remaining component of the MCP, and (d) fusing **cells produced** from steps (a)-(c) to form a hybrid **cell**, whereby the hybrid **cell** expresses the MCP. Also claimed is a method (B) for screening for successful fusion of a first **cell** containing a first NS encoding a desired **antibody heavy chain** and a second **cell** containing a second NS encoding a desired **antibody light chain**, comprising: (a) including a NS encoding a first marker gene in the first **cell** ; (b) including a NS encoding a second marker gene in the second **cell**; (c) fusing the first **cell** and the second **cell** under fuseogenic conditions to **produce** a fused **cell**, and (d) assaying for the presence of the first and second marker genes in the fused **cell**, whereby detection of the presence of the first and second marker genes in the fused **cell** indicates a successful fusion. Also claimed is a multi-component **protein produced** as in (A).

The marker genes are preferably the hygromycin resistance gene, the neomycin resistance (neo) gene, the hypoxanthine phosphoribosyl transferase gene, the **dihydrofolate reductase** (**DHFR**) gene, and the LacZ reporter gene. The method further comprises: (e) culturing the hybrid **cells** so as to express the multi-component **protein**, and (f) recovering the multi-component **protein** from the hybrid **cell** culture.The first and second **cells** are selected from mammalian, myeloma and non-lymphoid **cells**. The **protein** is an antibody.

USE - The method allows separately transformed **cells** to be individually selected for optimal expression of each component of the MCP. The method results in a final MCP product which is not expressed until a single hybrid **cell** is produced from the fusion of each **cell** expressing a component of the final **protein** product.

Dwg.0/10

L22 ANSWER 21 OF 24 MEDLINE on STN
ACCESSION NUMBER: 1999201274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10099478
TITLE: Clonal variability within **dihydrofolate reductase**-mediated gene amplified Chinese hamster ovary **cells**: stability in the absence of selective pressure.
AUTHOR: Kim N S; Kim S J; Lee G M

Searcher : Shears 571-272-2528

CORPORATE SOURCE: Department of Biological Sciences, Korea Advanced Institute of Science and Technology 373-1, Kusong-Dong, Yusong-Gu, Taejon 305-701, Korea.
SOURCE: Biotechnology and bioengineering, (1998 Dec 20) 60 (6) 679-88.
Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990517

AB Recombinant Chinese hamster ovary (rCHO) **cells** expressing a high level of chimeric antibody were obtained by cotransfection of heavy- and **light-chain** cDNA expression vectors into **dihydrofolate reductase**-deficient CHO **cells** and subsequent gene amplification in medium containing stepwise increments in methotrexate (MTX) level up to 1.0 microM. To determine the clonal variability within the amplified **cell** population in regard to **antibody production** stability, 20 subclones were randomly isolated from the amplified **cell** population at 1.0 microM MTX (CS13-1.0 **cells**). Clonal analysis showed that CS13-1.0 **cells** were heterogeneous with regard to specific growth rate (mu) and specific antibody productivity (qAb), although they were derived from a single clone. The mu and qAb of 20 subclones were in the range of 0.51 to 0.72 day-1 and 10.9 to 19.1 microgram/10(6) **cells**/day, respectively. During 8 weeks of cultivation in the absence of selective pressure, the mu of most subclones did not change significantly. On the other hand, their qAb decreased significantly. Furthermore, the relative decrease in qAb varied among subclones, ranging from 30% to 80%. Southern and Northern blot analyses showed that this decreased qAb resulted mainly from the loss of amplified immunoglobulin (Ig) gene copies and their respective cytoplasmic mRNAs. For the sake of screening convenience, an attempted was made to correlate the initial properties of subclones (such as mu, qAb, and Ig gene copies) with their **antibody production** stability during long-term culture. Among these initial properties examined, only qAb of subclones could help to predict their stability to some extent. The subclones with high qAb were relatively stable with regard to **antibody production** during long-term culture in the absence of selective pressure ($P < 0.005$, ANOVA). Taken together, the clonal heterogeneity in an amplified CHO **cell** population necessitates clonal analysis for screening stable clones with high qAb.

L22 ANSWER 22 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 3

ACCESSION NUMBER: 1997:130865 BIOSIS
DOCUMENT NUMBER: PREV199799422678
TITLE: Comparison of the **production** of a human monoclonal **antibody** against HIV-1 by heterohybridoma **cells** and recombinant CHO **cells**: A flow cytometric study.
AUTHOR(S): Borth, Nicole [Reprint author]; Strutzenberger, Karl; Donalies, Ute; Kunert, Renate; Katinger, Hermann

CORPORATE SOURCE: Inst. Applied Microbiol., Nussdorfer Laende 11, 1190 Vienna, Austria
SOURCE: Cytotechnology, (1996) Vol. 22, No. 1-3, pp. 129-138. ISSN: 0920-9069.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Mar 1997
Last Updated on STN: 25 Mar 1997

AB The **production** of human monoclonal **antibodies** for therapeutic use is of increasing importance for treatment of viral infections such as AIDS. As human x mouse heterohybridomas rarely reach the growth rates and **cell** specific production rates of mouse hybridomas the transfection of standard **cell** lines, such as CHO or BHK, is a promising alternative. This has the additional advantage that the IgG subtype can be changed to suit the desired application. However, the use of a **cell** line that has not originally developed to **produce antibodies** , as lymphocytes and myeloma **cells** have, might have unrecognised drawbacks. This will be especially significant in the case of antibodies as each molecule consists of 4 chains linked by disulphide bonds which require specific intracellular factors to be properly folded and processed (**Heavy chain** binding **protein, Protein** Disulfide Isomerase a.o.). In this study we have therefore compared two **cell** lines: a human x mouse heterohybridoma **producing** IAM-2F5, a human IgG-3 **antibody** specific for HIV-1 with neutralising properties and a Chinese Hamster Ovary **cell** transfected with **dihydrofolate reductase** and with the heavy and **light chain** genes of IAM-2F5 modified to IgG-1. From each **cell** line three subclones were selected with low, medium and high specific production rates. Batch cultures were performed and the following cellular parameters analysed by flow cytometry; 1) total RNA content (translational activity); 2) total **protein** content; 3) **cell** cycle phase distribution; 4) concentration of light and **heavy chains**; 5) concentration of helper **proteins** such as BiP and PDI. The production rate of heterohybridoma **cells** was best reflected in the intracellular concentration of kappa chain, while the gamma chain concentration was comparable for all three subclones. In the CHO **cells** the gamma chain expression and thus gene copy number appeared to be the limiting factor. The GRP78/BiP concentration in CHO remained unchanged in spite of a 5-fold higher concentration of gamma chain in the high producing subclone. The PDI concentration in CHO **cells** was much lower compared to the heterohybridoma **cells**, irrespective of production rates.

L22 ANSWER 23 OF 24 MEDLINE on STN

ACCESSION NUMBER: 94141203 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8308283

TITLE: A new vector for the high level expression of chimeric antibodies in myeloma **cells**.

AUTHOR: Shitara K; Nakamura K; Tokutake-Tanaka Y; Fukushima M; Hanai N
CORPORATE SOURCE: Division of Immunology, Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Japan.

SOURCE: Journal of immunological methods, (1994 Jan 3) 167 (1-2) 271-8.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19970203
Entered Medline: 19940311

AB We previously reported the expression of a mouse/human chimeric anti-ganglioside GD3 antibody, KM871 (IgG1,kappa) in mouse myeloma SP2/0 **cells** under the control of the ecotropic Moloney virus long terminal repeat by the co-transfection of chimeric heavy (H) and light (L) chain vectors (Shitara et al. (1993) Cancer Immunol. Immunother.). To establish an efficient and high level expression system for the chimeric antibody, we did comparative study on vector systems and host **cells**. An improved expression vector, named 'a tandem vector, pChi641HLGM4' was constructed, in which both of the chimeric H and L chain gene transcription units and a **dihydrofolate reductase** (**dhfr**) gene transcription unit were inserted. When two kinds of mouse myeloma **cell** lines, SP2/0 and P3U1, were used as host **cells**, frequency of the incidence of **antibody-producing** transfectants was markedly increased by the use of the tandem vector compared with the use of the mixture of each chimeric H vector and L chain vector. To select out appropriate host **cells**, transfection frequency and **antibody production** level were compared among SP2/0, P3U1 and rat myeloma YB2/0 **cells** by transfection of the tandem vector. YB2/0 **cell** was shown to have the highest potential in both the transfection frequency and the **antibody production** . Introduction of the tandem vector into YB2/0 **cells** and the subsequent amplification with 50-200 nM methotrexate gave rise to several clones that stably secreted 70-100 micrograms/10(6) **cells** per 24 h of the chimeric antibody. This productivity of the antibody is one of the highest levels which have been achieved by other investigators using transfected myeloma **cells**. Using this system it took only 2-3 months to establish the transfectant clones which stably **produced** the chimeric **antibody** .

L22 ANSWER 24 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 87116049 EMBASE
DOCUMENT NUMBER: 1987116049
TITLE: Reconstitution of functionally active antibody directed against creatine kinase from separately expressed heavy and **light chains** in non-lymphoid **cells**.
AUTHOR: Weidle U.H.; Borgya A.; Mattes R.; et al.
CORPORATE SOURCE: Boehringer Mannheim GmbH, Biochemical Research Center, D-8132 Tutzing, Germany
SOURCE: Gene, (1987) Vol. 51, No. 1, pp. 21-29.
CODEN: GENED6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
ENTRY DATE: Entered STN: 911211
Last Updated on STN: 911211

Searcher : Shears 571-272-2528

AB We report here for the first time reconstitution and secretion and functionally active antibody in non-lymphoid **cells**. Expression vectors for the light and the **heavy chain** of a monoclonal antibody directed against creatine kinase (EC 2.7.3.2) were introduced into COS and CHO Chinese hamster ovary **dhfr- cells**. Introduction of the expression vectors separately gave rise to immuno-reactive material in the culture supernatants, but only cotransfection of the expression plasmids resulted in secretion of **protein** with immuno-reactivity against antibodies directed against mouse heavy and **light chains** as well as specific antigen-binding affinity, as determined by enzyme-linked immunosorbent assay. Secreted κ and γ chains from reconstituted antibody were characterized by immunoadsorption and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. In COS **cells**, reconstituted antibody was transiently secreted; cotransfection of κ and γ chain expression plasmids with a **dihydrofolate reductase** (**DHFR**)-expression plasmid into CHO **dhfr- cells** gave rise to stable transformants secreting functionally active antibody.

FILE 'MEDLINE' ENTERED AT 17:01:27 ON 11 JAN 2006

FILE LAST UPDATED: 10 JAN 2006 (20060110/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

L23	64412	SEA	FILE=MEDLINE	ABB=ON PLU=ON	ANTIBODIES/CT
L24	4652	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ADENOSINE DEAMINASE"/CT
L25	4007	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26	34	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L23 AND (L24 OR L25)
L27	4276	SEA	FILE=MEDLINE	ABB=ON PLU=ON	CELLS/CT
L28	0	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L26 AND L27

L23	64412	SEA	FILE=MEDLINE	ABB=ON PLU=ON	ANTIBODIES/CT
L24	4652	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"ADENOSINE DEAMINASE"/CT
L25	4007	SEA	FILE=MEDLINE	ABB=ON PLU=ON	"TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26	34	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L23 AND (L24 OR L25)
L29	118802	SEA	FILE=MEDLINE	ABB=ON PLU=ON	PROTEINS/CT
L30	84572	SEA	FILE=MEDLINE	ABB=ON PLU=ON	PEPTIDES/CT
L31	1	SEA	FILE=MEDLINE	ABB=ON PLU=ON	L26 AND (L29 OR L30)

Searcher : Shears 571-272-2528

L31 ANSWER 1 OF 1 MEDLINE on STN
ACCESSION NUMBER: 95349954 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7624146
TITLE: Preferential detection of catalytically inactive c-erbB-2 by antibodies to unphosphorylated peptides mimicking receptor tyrosine autophosphorylation sites.
AUTHOR: Epstein R J
CORPORATE SOURCE: Division of Cell, Molecular and Oncology Research, Charing Cross & Westminster Medical School, University of London, UK.
SOURCE: Oncogene, (1995 Jul 20) 11 (2) 315-23.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950911
Last Updated on STN: 20000303
Entered Medline: 19950831

ED Entered STN: 19950911
Last Updated on STN: 20000303
Entered Medline: 19950831

AB The c-erbB-2 tyrosine kinase is often overexpressed in human breast cancer, but correlations of receptor expression with tumour behaviour have proven elusive in patients without metastases at diagnosis. To address the possibility that receptor function may be more informative than expression, we previously developed function-specific c-erbB-2 antibodies using synthetic tyrosine-phosphorylated peptide immunogens (Epstein et al., Proc. Natl. Acad. Sci. USA 1992; 89: 10435-10439). Here the converse approach has been taken to determine the functional status of c-erbB-2 receptors detected by antibodies to dephosphorylated (dep) autophosphorylation sequences. In contrast to antiphosphopeptide (apt) antibodies, dep antibodies to the Tyr1248 autophosphorylation site exhibited preferential, but not exclusive, binding to tyrosine-dephosphorylated c-erbB-2. Consistent with this, catalytically active and inactive receptors could not be clearly distinguished by in vitro autophosphorylation experiments in which c-erbB-2 was immunoprecipitated using a monoclonal Tyr1248 dep antibody. A dep antiserum recognizing autophosphorylation sites N-terminal to Tyr1248 exclusively recognized tyrosine-dephosphorylated c-erbB-2 following antibody preabsorption with homologous phosphopeptides. Although indirect, these data are consistent with a model of sequential c-erbB-2 autophosphorylation in which Tyr1248 is the final residue modified. Moreover, since many studies of c-erbB-2 expression have used antibodies to dephosphorylated autophosphorylation sites, these results caution against automatically equating such receptor immunoreactivity with in vivo function or clinical significance.

FILE 'HOME' ENTERED AT 17:05:59 ON 11 JAN 2006

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=> d his ful

     (FILE 'HOME' ENTERED AT 16:39:00 ON 11 JAN 2006)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 16:43:41 ON 11 JAN 2006
               E DIHYDROFOLATE REDUCTASE/CN 5
L1          268 SEA ABB=ON  PLU=ON  DIHYDROFOLATE REDUCTASE?/CN
               E GLUTAMINE SYNTHASE/CN 5
L2           17 SEA ABB=ON  PLU=ON  GLUTAMINE SYNTHASE?/CN
               E ADENOSINE DEAMINASE/CN 5
L3          123 SEA ABB=ON  PLU=ON  ADENOSINE DEAMINASE?/CN
L4          408 SEA ABB=ON  PLU=ON  L1 OR L2 OR L3

     FILE 'HCAPLUS' ENTERED AT 16:44:35 ON 11 JAN 2006
L5        37197 SEA ABB=ON  PLU=ON  L4 OR DHFR OR GS OR (DIHYDROFOLATE OR
               DI(W)(HYDROFOLATE OR HYDRO FOLATE) OR DIHYDRO FOLATE)(W)(RE
               DUCTASE OR DEHYDROGENASE OR DE HYDROGENASE) OR GLUTAMINE
               SYNTHASE OR ADENOSINE(W)(DEAMINASE OR DE AMINASE OR
               AMINOHYDROLASE OR AMINO HYDROLASE)
L6          831 SEA ABB=ON  PLU=ON  (TETRAHYDROFOLATE OR TETRA(W)(HYDROFOLA
               TE OR HYDRO FOLATE) OR TETRAHYDRO FOLATE)(W)(DEHYDROGENASE
               OR DE HYDROGENASE) OR FOLIC(1W)REDUCTASE
L7         2000 SEA ABB=ON  PLU=ON  (L5 OR L6) AND ANTIBOD?
               D QUE
L8          144 SEA ABB=ON  PLU=ON  L7 AND (LIGHT CHAIN OR LC)
L9           99 SEA ABB=ON  PLU=ON  L8 AND (HEAVY CHAIN OR HC)
L10          93 SEA ABB=ON  PLU=ON  L9 AND CELL
L11           6 SEA ABB=ON  PLU=ON  L9 AND (MYELOMA OR NSO OR NS0 OR
               HYBRID)(3A)CELL
               D KWIC
L12          40 SEA ABB=ON  PLU=ON  L10 AND (PRODUCING OR PRODUCE# OR
               PRODUCTION OR MANUF?)
L13           0 SEA ABB=ON  PLU=ON  L12 AND (POLYNUCLEOTIDE OR POLY
               NUCLEOTIDE)
L14          31 SEA ABB=ON  PLU=ON  L12 AND (POLYPEPTIDE OR POLYPROTEIN OR
               PROTEIN OR PEPTIDE)
               D QUE
L*** DEL  90515 S (PRODUCING OR PRODUCE# OR PRODUCTION OR MANUF?)(L)ANTIBOD
               D KWIC
L*** DEL    419 S L15 AND (L5 OR L6)
L*** DEL     40 S L12 AND (LIGHT CHAIN OR LC)
L*** DEL     50 S L16 AND (LIGHT CHAIN OR LC)
L*** DEL     48 S L16 AND (HEAVY CHAIN OR HC)
L*** DEL     40 S L17 AND (HEAVY CHAIN OR HC)
L*** DEL     39 S L18 AND CELL
               D KWIC
               D KWIC 2
L15       52430 SEA ABB=ON  PLU=ON  (PRODUCING OR PRODUCE# OR PRODUCTION
               OR MANUF?)(S)ANTIBOD?
               D KWIC
L16         257 SEA ABB=ON  PLU=ON  L15 AND (L5 OR L6 OR GLUTAMINE
               SYNTHETASE)
L17          46 SEA ABB=ON  PLU=ON  L16 AND (LIGHT CHAIN OR LC)
L18          38 SEA ABB=ON  PLU=ON  L17 AND (HEAVY CHAIN OR HC)
               D QUE
               D KWIC
L19          37 SEA ABB=ON  PLU=ON  L18 AND CELL
               D KWIC
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                D KWIC 2
                D KWIC 3
                D QUE
L20           28 SEA ABB=ON  PLU=ON  L19 AND (POLYPROTEIN OR POLYPEPTIDE OR
                PEPTIDE OR PROTEIN)
L*** DEL       0 S L20 AND HORI ?/AU
L*** DEL       0 S L20 AND DAVIS ?/AU
L*** DEL       1 S (HORI ? AND DAVIS ?)/AU
                D TI AU
                D .BEVSTR1

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 16:57:46 ON 11 JAN 2006
L21           30 SEA ABB=ON  PLU=ON  L20
L22           24 DUP REM L21 (6 DUPLICATES REMOVED)

     FILE 'REGISTRY' ENTERED AT 17:01:15 ON 11 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 17:01:15 ON 11 JAN 2006
                D QUE L20
                D L20 1-28 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 17:01:20 ON 11 JAN 2006
                D L22 1-24 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 17:01:27 ON 11 JAN 2006
                E ANTIBODIES/CT 5
L23        64412 SEA ABB=ON  PLU=ON  ANTIBODIES/CT
                E ADENOSINE DEAMINASE/CT 5
L24         4652 SEA ABB=ON  PLU=ON  "ADENOSINE DEAMINASE"/CT
                E GLUTAMINE SYNTHASE/CT 5
                E TETRAHYDROFOLATE DEHYDROGENASE/CT 5
L25         4007 SEA ABB=ON  PLU=ON  "TETRAHYDROFOLATE DEHYDROGENASE"/CT
L26           34 SEA ABB=ON  PLU=ON  L23 AND (L24 OR L25)
                E CELLS/CT 5
L27         4276 SEA ABB=ON  PLU=ON  CELLS/CT
L28            0 SEA ABB=ON  PLU=ON  L26 AND L27
                E POLYPEPTIDES/CT 5
                E POLYPEPTIDE/CT 5
                E POLYPROTEIN/CT 5
                E PROTEINS/CT 5
L29       118802 SEA ABB=ON  PLU=ON  PROTEINS/CT
                E PEPTIDES/CT 5
L30        84572 SEA ABB=ON  PLU=ON  PEPTIDES/CT
L31            1 SEA ABB=ON  PLU=ON  L26 AND (L29 OR L30)
                D QUE L28
                D QUE L31
                D L31 .BEVERLYMED

     FILE 'HOME' ENTERED AT 17:05:59 ON 11 JAN 2006


     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   10 JAN 2006  HIGHEST RN 871658-99-0
     DICTIONARY FILE UPDATES:  10 JAN 2006  HIGHEST RN 871658-99-0

                    Searcher    :     Shears     571-272-2528
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 11 Jan 2006 VOL 144 ISS 3
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 10 JAN 2006 (20060110/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht

Searcher : Shears 571-272-2528

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 4 January 2006 (20060104/ED)

FILE EMBASE
FILE COVERS 1974 TO 6 Jan 2006 (20060106/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 6 JAN 2006 <20060106/UP>
MOST RECENT DERWENT UPDATE: 200602 <200602/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classif

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html <

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

FILE SCISEARCH

FILE COVERS 1974 TO 4 Jan 2006 (20060104/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 10 JAN 2006 (20060110/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 02 JAN 2006 <20060102/UP>
FILE COVERS APR 1973 TO SEPTEMBER 29, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html <

FILE HOME

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FILE COVERS 1907 - 11 Jan 2006 VOL 144 ISS 3
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L1 268 SEA FILE=REGISTRY ABB=ON PLU=ON DIHYDROFOLATE REDUCTASE?/CN
L2 17 SEA FILE=REGISTRY ABB=ON PLU=ON GLUTAMINE SYNTHASE?/CN
L3 123 SEA FILE=REGISTRY ABB=ON PLU=ON ADENOSINE DEAMINASE?/CN
L4 408 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2 OR L3
L5 37197 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 OR DHFR OR GS OR (DIHYDROFOLATE OR DI(W)(HYDROFOLATE OR HYDRO FOLATE) OR DIHYDRO FOLATE)(W)(REDUCTASE OR DEHYDROGENASE OR DE HYDROGENASE) OR GLUTAMINE SYNTHASE OR ADENOSINE(W)(DEAMINASE OR DE AMINASE OR AMINOHYDROLASE OR AMINO HYDROLASE)
L6 831 SEA FILE=HCAPLUS ABB=ON PLU=ON (TETRAHYDROFOLATE OR TETRA(W)(HYDROFOLATE OR HYDRO FOLATE) OR TETRAHYDRO FOLATE)(W)(DEHYDROGENASE OR DE HYDROGENASE) OR FOLIC(1W)REDUCTASE
L15 52430 SEA FILE=HCAPLUS ABB=ON PLU=ON (PRODUCING OR PRODUCE# OR PRODUCTION OR MANUF?)(S)ANTIBOD?
L16 257 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (L5 OR L6 OR GLUTAMINE SYNTHETASE)
L17 46 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 AND (LIGHT CHAIN OR LC)
L18 38 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND (HEAVY CHAIN OR HC)
L19 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 AND CELL
L20 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L19 AND (POLYPROTEIN OR POLYPEPTIDE OR PEPTIDE OR PROTEIN)

L20 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 09 Nov 2005
ACCESSION NUMBER: 2005:1190118 HCAPLUS
TITLE: Bi-cistronic expression of anti-HBsAg based on Flp recombination targeting and IRES sequence
AUTHOR(S): Ruan, Chengmai; Zhao, Jinhong; An, Xiaoping; Li, Jianmin; Hao, Xiaomeng; Tong, Yigang; Chen, Wei; Wang, Haitao
CORPORATE SOURCE: Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, 100071, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (2004), 28(5), 427-429
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The expression efficiency of whole antibodies that are different in construction was compared. A bi-cistronic antibody expression vector was constructed that included FLP recombination site and ECMV-IRES sequence. The **light chain** was inserted up-streamly to the IRES site, and in down-stream multi-cloning site, the **heavy chain** was inserted. The construct was

transfected into CHO/**dhfr cell** with LipofectAMINE. In transient expression, no detectable **antibody** expression was **produced** in ELISA assay, but in stable clone selected with blamycin, the **antibody** was detected, and the expression variance was less than 40%. It was proved that the construct is a promising tool for **protein** expression level comparing.

L20 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 07 Oct 2005
ACCESSION NUMBER: 2005:1078101 HCAPLUS
DOCUMENT NUMBER: 143:365642
TITLE: Retroviral vectors comprising exogenous promoter and amplifiable marker for integrating into host **cell** chromosome to produce recombinant **protein** or immunoglobulin
INVENTOR(S): Bleck, Gregory T.
PATENT ASSIGNEE(S): Cardinal Health Pts, Llc, USA
SOURCE: U.S. Pat. Appl. Publ., 142 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005221429	A1	20051006	US 2005-36557		20050114
PRIORITY APPLN. INFO.:			US 2004-537462P	P	20040116

AB The present invention relates to the production of **proteins** in host **cells**, and more particularly to host **cells** containing multiple integrated copies of an integrating vector comprising an exogenous gene and an amplifiable marker. The amplifiable marker is selected from **DHFR** and **glutamine synthetase**. The exogenous gene or transgene comprises signal sequence, MoMLV element, IRES element, polycistronic sequence and/or gene encoding IgG, IgA, IgM, IgD, IgE or sIg. The host **cell** is selected from CHO **cell**, baby hamster kidney **cell**, human 293 **cell** and bovine mammary epithelial **cell**. The present invention further provides methods of expressing increased levels of recombinant **protein** in host **cells** using such vectors.

IT **9002-03-3, Dihydrofolate reductase**
9023-70-5, Glutamine synthetase
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(retroviral vectors comprising exogenous promoter and amplifiable marker for integrating into host **cell** chromosome to produce recombinant **protein** or Ig)

L20 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 29 Jul 2005
ACCESSION NUMBER: 2005:672773 HCAPLUS
DOCUMENT NUMBER: 143:152011
TITLE: Overexpression of enzymes involved in post-translational **protein** modifications in human **cells**
INVENTOR(S): Uytdehaag, Alphonsus G. C. M.; Opstelten, Dirk J. E.

PATENT ASSIGNEE(S): Neth.
SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Ser. No. 497,832.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005164386	A1	20050728	US 2004-26518	20041230
US 6855544	B1	20050215	US 2000-549463	20000414
WO 2003048348	A2	20030612	WO 2002-NL804	20021209
WO 2003048348	A3	20031211		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005181359	A1	20050818	US 2005-102073	20050408

PRIORITY APPLN. INFO.:

US 1999-129452P	P	19990415
US 2000-549463	A2	20000414
WO 2002-NL804	W	20021209
US 2005-497832	A2	20050110
WO 2001-NL792	A	20011029
WO 2001-NL892	A	20011207
EP 2002-75327	A	20020125
WO 2002-NL257	A	20020419
WO 2002-NL686	W	20021029
US 2004-494140	A2	20040429
US 2004-26518	A2	20041230

AB Methods and compns. for the production of recombinant **proteins** in a human **cell** line are provided. The methods and compns. are particularly useful for generating stable expression of human recombinant **proteins** of interest that are modified post-translationally, for example, by glycosylation. Such **proteins** may have advantageous properties in comparison with their counterparts produced in non-human systems such as Chinese hamster ovary **cells**. Immortalized human embryonic retina **cells** (PER.C6) comprising a nucleic acid sequence encoding an adenoviral E1A **protein** integrated into the genome of the

cells and a nucleic acid sequence encoding an enzyme involved in post-translational modification of **proteins**, wherein said nucleic acid sequence encoding the enzyme involved in post-translational modification of **proteins** is under control of a heterologous promoter are further disclosed. Over-expression of E1B **protein** acts to inhibit apoptosis. Methods for production of recombinant **proteins** from such **cells** and obtaining such recombinant **proteins** having increased sialylation are provided by recombinant co-expression of α-2,6-sialyltransferase or α-2,3-sialyltransferase. Increase of sialic acid content in recombinantly produced erythropoietin results in an increased erythropoietic activity.

IT **9002-03-3P, Tetrahydrofolate Dehydrogenase**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(recombinant **protein** production in human **cell** PER.C6 transformed with adenoviral E1 **protein** genes)

L20 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 27 May 2005
ACCESSION NUMBER: 2005:453802 HCAPLUS
DOCUMENT NUMBER: 142:476236
TITLE: **Protein** A or other lymphocyte differentiation factor for immunomodulation, compositions and methods of use
INVENTOR(S): Mann, Paul
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 121,481.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005113299	A1	20050526	US 2004-941636	20040915
US 2003211986	A1	20031113	US 2002-121481	20020410
WO 2003086317	A2	20031023	WO 2003-US7019	20030306
WO 2003086317	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 2002-121481	A2	20020410
WO 2003-US7019	A2	20030306

AB Methods and compns. for modulating an immune response in a subject are provided. Methods include administering to the subject a composition comprising an effective amount of a lymphocyte differentiation factor,

e.g., **protein** A (PA), sufficient to modulate the immune response. Compns. include a lymphocyte differentiation factor, e.g., PA, in an amount less than 1 μg. PA administered at very low concns. reduced inflammation and inhibited or reversed tissue damage caused by the inflammation in arthritis animal models.

IT **9026-93-1, Adenosine deaminase**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(deficiency, treatment of; **protein** A or other lymphocyte differentiation factor for immunomodulation)

L20 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 21 Jan 2005
ACCESSION NUMBER: 2005:58349 HCAPLUS
DOCUMENT NUMBER: 142:128717
TITLE: Episomal replication-competent transient expression vectors for eukaryotic hosts including a scaffold attachment region
INVENTOR(S): Ivanova, Lidia; Saudan, Philippe
PATENT ASSIGNEE(S): Cytos Biotechnology AG, Switz.
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005005644	A1	20050120	WO 2004-EP7556	20040709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005064467	A1	20050324	US 2004-888961	20040712
PRIORITY APPLN. INFO.:			US 2003-486238P P	20030711
			US 2003-524852P P	20031126
			WO 2004-EP7556 A	20040709

AB Transient expression plasmid vectors for eukaryotic **cells** that can drive high levels of expression are described. These vectors may be used for the short term, high-level expression of a foreign gene, e.g. in the treatment of disease (no data.). The plasmids carry one or more replication origins and one or more genes for replication initiation factors. They also carry a scaffold/matrix attachment region (S/MAR), preferably derived from the interferon β gene. Inclusion of the matrix attachment region greatly increases the level of expression of genes borne by the vector. Expression is driven by a strong promoter and the expression cassette contains other elements

that improve levels or stability of the transcript. Use of oriP and the EBNA1 gene of Epstein-Barr virus to make the plasmid replication competent is demonstrated.

IT **9023-70-5, Glutamine synthetase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (gene for, as marker in expression vectors; episomal replication-competent transient expression vectors for eukaryotic hosts including scaffold attachment region)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 03 Dec 2004
ACCESSION NUMBER: 2004:1038669 HCAPLUS
DOCUMENT NUMBER: 142:22311
TITLE: Mouse/human chimeric anti-phencyclidine antibody for treating arylcyclohexylamine drug abuse or overdose
INVENTOR(S): Owens, S. Michael; Lacy, H. Marie
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004242848	A1	20041202	US 2004-828782		20040421
PRIORITY APPLN. INFO.:			US 2003-464190P	P	20030421

AB The present invention provides a chimeric mouse/human antibody (ch-mAb6B5) for treatment of abuse and toxicity of the arylcyclohexylamines class of drugs (i.e., phencyclidine- or PCP-like drugs). This antibody comprises light and **heavy chain** PCP binding regions of mouse mAb6B5, coupled to the light and **heavy chain** constant regions of a human kappa IgG2 or IgG4 isoform. Also provided are the DNA and amino acid sequences of the chimeric light and **heavy chain** of this antibody. Further provided are data that demonstrate that the new chimeric antibody retains the high affinity and specificity of a previously generated mouse anti-PCP monoclonal antibody (mAb6B5) yet being minimally immunogenic since it has human Ig constant region. This new medication would allow safe and effective treatment of PCP drug overdose, decrease mortality, and reduce harmful effects due to excessive and prolonged PCP drug use.

L20 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 26 Nov 2004
ACCESSION NUMBER: 2004:1019664 HCAPLUS
DOCUMENT NUMBER: 142:1781
TITLE: Production of host **cells** containing multiple integrating retroviral vectors by serial transduction
INVENTOR(S): Bleck, Gregory T.; Bremel, Robert D.; Miller, Linda U.
PATENT ASSIGNEE(S): Gala Design, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 143 pp., Cont.-in-part of U.S. Ser. No. 397,079.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004235173	A1	20041125	US 2004-759315	20040116
US 2003092882	A1	20030515	US 2001-897511	20010629
US 6852510	B2	20050208		
US 2003224415	A1	20031204	US 2003-397079	20030326
US 2005100952	A1	20050512	US 2004-18895	20041221
WO 2005072129	A2	20050811	WO 2005-US1165	20050114

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 2000-215925P	P	20000703
US 2001-897511	A2	20010629
US 2003-397079	A2	20030326
US 2002-368357P	P	20020328
US 2004-759315	A	20040116

AB The present invention relates to the production of **proteins** in host **cells**, and more particularly to host **cells** containing multiple integrated copies of an integrating vector comprising an exogenous gene and methods of making such host **cells** by serial transduction or transfection. The present invention further provides methods of expressing increased levels of **protein** in host **cells** using such vectors.

IT **9002-03-3P, Dihydrofolate reductase**
9023-70-5P, Glutamine synthetase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(as amplifiable marker; production of host **cells** containing multiple integrating retroviral vectors by serial transduction)

L20 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Nov 2004
ACCESSION NUMBER: 2004:977360 HCAPLUS
DOCUMENT NUMBER: 142:154330
TITLE: Comparative proteomic analysis of **GS**-NSO murine myeloma **cell** lines with varying recombinant monoclonal **antibody**

production rate
AUTHOR(S): Smales, C. M.; Dinnis, D. M.; Stansfield, S. H.; Alete, D.; Sage, E. A.; Birch, J. R.; Racher, A. J.; Marshall, C. T.; James, D. C.
CORPORATE SOURCE: Research School of Biosciences, University of Kent, Canterbury, CT2 7NJ, UK
SOURCE: Biotechnology and Bioengineering (2004), 88(4), 474-488
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have employed an inverse engineering strategy based on quant. proteome anal. to identify changes in intracellular **protein** abundance that correlate with increased specific recombinant monoclonal **antibody production** (qMab) by engineered murine myeloma (NSO) **cells**. Four homogeneous NSO **cell** lines differing in qMab were isolated from a pool of primary transfectants. The proteome of each stably transfected **cell** line was analyzed at mid-exponential growth phase by two-dimensional gel electrophoresis (2D-PAGE) and individual **protein** spot volume data derived from digitized gel images were compared statistically. To identify changes in **protein** abundance associated with qMab datasets were screened for **proteins** that exhibited either a linear correlation with **cell** line qMab or a conserved change in abundance specific only to the **cell** line with highest qMab. Several **proteins** with altered abundance were identified by mass spectrometry. **Proteins** exhibiting a significant increase in abundance with increasing qMab included mol. chaperones known to interact directly with nascent Igs during their folding and assembly (e.g., BiP, endoplasmin, **protein** disulfide isomerase). 2D-PAGE anal. showed that in all **cell** lines Mab **light chain** was more abundant than **heavy chain**, indicating that this is a likely prerequisite for efficient Mab production In summary, these data reveal both the adaptive responses and mol. mechanisms enabling mammalian **cells** in culture to achieve high-level recombinant monoclonal **antibody production**
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Nov 2004
ACCESSION NUMBER: 2004:973454 HCAPLUS
DOCUMENT NUMBER: 142:92297
TITLE: On the Optimal Ratio of Heavy to **Light Chain** Genes for Efficient Recombinant **Antibody Production** by CHO **Cells**
AUTHOR(S): Schlatter, Stefan; Stansfield, Scott H.; Dinnis, Diane M.; Racher, Andrew J.; Birch, John R.; James, David C.
CORPORATE SOURCE: School of Engineering, University of Queensland, 4072, Australia
SOURCE: Biotechnology Progress (2005), 21(1), 122-133
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monoclonal antibodies (Mab) are heterotetramers consisting of an equimolar ratio of **heavy chain** (**HC**) and **light chain** (**LC**) **polypeptides**. Accordingly, most recombinant Mab expression systems utilize an equimolar ratio of **heavy chain** (**hc**) to **light chain** (**lc**) genes encoded on either one or two plasmids. However, there is no evidence to suggest that this gene ratio is optimal for stable or transient production of recombinant Mab. In this study we have determined the optimal ratio of **hc**:**lc** genes for production of a recombinant IgG4 Mab, cB72.3, by Chinese hamster ovary (CHO) **cells** using both empirical and math. modeling approaches. Polyethyleneimine-mediated transient expression of cB72.3 at varying ratios of **hc**:**lc** genes encoded on sep. plasmids yielded an optimal Mab titer at a **hc**:**lc** gene ratio of 3:2; a conclusion confirmed by sep. math. modeling of the Mab folding and assembly process using transient expression data. On the basis of this information, we hypothesized that utilization of **hc** genes at low **hc**:**lc** gene ratios is more efficient. To confirm this, cB72.3 Mab was transiently produced by CHO **cells** at constant **hc** and varying **lc** gene dose. Under these conditions, Mab yield was increased with a concomitant increase in **lc** gene dose. To determine if the above findings also apply to stably transfected CHO **cells** producing recombinant Mab, we compared the intra- and extracellular ratios of **HC** and **LC polypeptides** for three **GS**-CHO **cells** lines transfected with a 1:1 ratio of **hc**:**lc** genes and selected for stable expression of the same recombinant Mab, cB72.3. Intra- and extracellular **HC**:**LC polypeptide** ratios ranged from 1:2 to 1:5, less than that observed on transient expression of the same Mab in parental CHO **cells** using the same vector. In conclusion, our data suggest that the optimal ratio of **hc**:**lc** genes used for transient and stable expression of Mab differ. In the case of the latter, we infer that optimal Mab production by stably transfected **cells** represents a compromise between **HC** abundance limiting productivity and the requirement for excess **LC** to render Mab folding and assembly more efficient.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 11 Nov 2004
ACCESSION NUMBER: 2004:958651 HCAPLUS
DOCUMENT NUMBER: 142:149757
TITLE: Bicistronic expression vector for animal **cells**, transformed **cell** line containing the same vector and method for **producing antibody proteins** using the same
INVENTOR(S): Jang, Hyeon Suk; Jung, Jong Geun; Park, U. Yeong; Ra, Geun Bae; Sim, Dong Seop; Yang, Jae Yeong; Yoo, Jin San; Yoon, Hye Seong
PATENT ASSIGNEE(S): Lg Life Sciences Ltd., S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7

DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2003062118	A	20030723	KR 2002-2544	20020116
PRIORITY APPLN. INFO.:			KR 2002-2544	20020116

AB A bicistronic expression vector for animal **cells**, a transformed **cell** line containing the same vector and a method for **producing antibody proteins** using the same are provided, thereby effectively expressing various genes such as an antigen gene. A bicistronic expression vector for animal **cells** comprises a cytomegalovirus (CMV) promoter required for **producing** the transcriptional RNA, at least one foreign gene selected from **light chain** gene or **heavy chain** gene of an **antibody**, an IRES sequence, a selective gene and a poly(A) sequence, sequentially, wherein the selective gene is dihydroxyfolate reductase (**DHFR**) or neomycin resistance gene (NEOR); the bicistronic expression vector is selected from pLCM-MoK(KCTC 10151BP), pLCD-MoK(KCTC 10151BP), pLCN-MoH(KCTC 10150BP) and pANTIBODY(KCTC 10152BP). A transformed animal **cell** is produced by transformation with the bicistronic expression vector. A method for **producing** the foreign gene selected from the **light chain** or **heavy chain** of the **antibody** is characterized by culturing the transformed animal **cell**.

L20 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 27 Jun 2004
ACCESSION NUMBER: 2004:515705 HCAPLUS
DOCUMENT NUMBER: 141:66202
TITLE: Method for producing recombinant **protein** with high efficacy
INVENTOR(S): Saudan, Philippe; Hennecke, Frank; Bachmann, Martin F.; Stern, Dorothee M.
PATENT ASSIGNEE(S): Cytos Biotechnology Ag, Switz.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004053137	A2	20040624	WO 2003-CH810	20031210
WO 2004053137	A3	20040812		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,

DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-432245P P 20021211

AB The present invention relates to the field of gene expression technol. and the production of recombinant **polypeptides** and/or untranslated RNA mols. in host **cells**. In particular, the invention provides a method for the production of recombinant **polypeptides** and/or untranslated RNA mols. in host **cells** allowing the production of high amts. of those mols. in a very short time and with a high degree of reproducibility, in particular with respect to a, preferably, pre-defined standard and, thus, making the present invention particularly attractive for the production of **proteins** for clin. use and the production under Good Manufacturing Practice (GMP).

IT **9023-70-5, Glutamine synthetase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as selection marker; method for producing recombinant **protein** with high efficacy)

L20 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 18 Jun 2004
ACCESSION NUMBER: 2004:493884 HCAPLUS
DOCUMENT NUMBER: 141:48565
TITLE: Mutant neomycin phosphotransferase genes and method for the selection of high-producing recombinant **cells**
INVENTOR(S): Enenkel, Barbara; Sautter, Kerstin; Otto, Ralf; Fieder, Juergen; Bergemann, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050884	A2	20040617	WO 2003-EP13203	20031125
WO 2004050884	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10330686	A1	20040617	DE 2003-10330686	20030708
CA 2507664	AA	20040617	CA 2003-2507664	20031125
EP 1567652	A2	20050831	EP 2003-812157	20031125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003016525 A 20051004 BR 2003-16525 20031125
PRIORITY APPLN. INFO.: DE 2002-10256081 A 20021129
DE 2003-10330686 A 20030708
WO 2003-EP13203 W 20031125

AB The invention relates to novel modified neomycin phosphotransferase genes and the use thereof in a selection method for high-producing recombinant **cells**. The invention also relates to expression vectors containing a modified neomycin phosphotransferase gene and a gene of interest functionally fused to an heterologous promoter, and a method for producing heterologous gene products by using said expression vectors. Thus, numerous mutant neomycin phosphotransferase genes were created which encoded enzymes with decreased activity. CHO **cells** cotransformed with IgG2 **light chain** expression plasmid containing D227G neomycin phosphotransferase mutant gene as selectable marker and IgG2 **heavy chain** expression plasmid containing GFP and **DHFR** genes were selected with G418 and sorted by FACS then amplified using methotrexate. Pools with productivity of 20 pg IgG2 per **cell** per day were obtained.

IT **9002-03-3, Dihydrofolate reductase**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(clone amplification using; mutant neomycin phosphotransferase genes and method for selection of high-producing recombinant **cells**)

L20 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 May 2004
ACCESSION NUMBER: 2004:390266 HCAPLUS
DOCUMENT NUMBER: 140:405477
TITLE: Chimeric and humanized mouse monoclonal anti-human IL-6 antibody CLB-8 and fragments for treatment of immune disease, infection and cancer
INVENTOR(S): Giles-Komar, Jill; Knight, David; Peritt, David; Trikha, Mohit
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039826	A1	20040513	WO 2002-US36213	20021026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2467719	AA	20030513	CA 2002-2467719	20021026
BR 2002014168	A	20040914	BR 2002-14168	20021026
EP 1562968	A1	20050817	EP 2002-784436	20021026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
NO 2004002418	A	20040805	NO 2004-2418	20040610
PRIORITY APPLN. INFO.:			US 2001-332437P P	20011114
			US 2001-332743P P	20011114
			WO 2002-US36213 W	20021026

AB The present invention relates to at least one novel chimeric, humanized or CDR-grafted anti-IL-6 antibodies derived from the murine CLB-8 antibody, including isolated nucleic acids that encode at least one such anti-IL-6 antibody, vectors, host **cells**, transgenic animals or plants, methods of making and using thereof, including therapeutic compns., methods and devices.

IT **9002-03-3, Dihydrofolate reductase**
9023-70-5, Glutamine synthetase
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene; chimeric and humanized mouse monoclonal anti-human IL-6 antibody CLB-8 and fragments for treatment of immune disease, infection and cancer)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 20 Feb 2004
ACCESSION NUMBER: 2004:141669 HCAPLUS
DOCUMENT NUMBER: 140:216171
TITLE: Anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers
INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schulke, Norbert; Gardner, Jason; Ma, Dangshe
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 151 pp., Cont.-in-part of Appl. No. PCT/US02/33944.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004033229	A1	20040219	US 2003-395894	20030321
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,				

NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004161776	A1	20040819	US 2003-695667		20031027
US 2005215472	A1	20050929	US 2004-976352		20041027
PRIORITY APPLN. INFO.:			US 2001-335215P	P	20011023
			US 2002-362747P	P	20020307
			US 2002-412618P	P	20020920
			WO 2002-US33944	A2	20021023
			US 2003-395894	A2	20030321
			US 2003-695667	A2	20031027

AB The invention includes **antibodies** or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of prostate specific membrane antigen (PSMA), compns. containing one or a combination of such **antibodies** or antigen-binding fragments thereof, hybridoma **cell** lines that **produce** the **antibodies**, and methods of using the **antibodies** or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA **proteins**, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers)

L20 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 31 Oct 2003
ACCESSION NUMBER: 2003:855544 HCAPLUS
DOCUMENT NUMBER: 139:346767
TITLE: Increasing yields of **proteins** manufactured by expression of the cloned gene using **cells** carrying multiple copies of stable plasmid carrying multiple expression cassettes
INVENTOR(S): Horwitz, Arnold H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 133 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003203447	A1	20031030	US 2003-404724	20030331
CA 2492008	AA	20040422	CA 2003-2492008	20030331
WO 2004033693	A1	20040422	WO 2003-US10154	20030331

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1492874	A1	20050105	EP 2003-808015 20030331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005528925	T2	20050929	JP 2004-543182 20030331
PRIORITY APPLN. INFO.:			US 2002-368530P P 20020329
			WO 2003-US10154 W 20030331

AB A method of increasing the yield of a foreign **protein** from a producer **cell** using multiple copies of a vector carrying several copies of an expression cassette is described. Plasmids carrying multiple expression cassettes are stabilized against loss by internal recombination by placing selectable markers between the expression cassettes. The method is particularly useful for the manufacture of Igs, especially Igs with light and **heavy chains** from different sources. Copy number may be increased by repeated transformation of the host **cell** carrying the same expression cassettes, but with different selectable markers. The expression cassettes using strong promoters appropriate for high level gene expression in the host **cell**. The development of CHO-derived **cell** lines producing high levels of bactericidal/permeability-increasing **proteins** using three rounds of transformation and selection is demonstrated.

IT **9026-93-1, Adenosine deaminase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for, as selectable marker; increasing yields of **proteins** manufactured by expression of cloned gene by increasing copy nos. of plasmid carrying multiple expression cassettes)

L20 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 09 Sep 2003
ACCESSION NUMBER: 2003:703715 HCAPLUS
DOCUMENT NUMBER: 140:13549
TITLE: Expression of whole human anti-HAV antibody in CHO **cells**
AUTHOR(S): Yu, Changming; Xu, Jing; Tong, Yigang; Chen, Wei; Liu, Guoqi; Xu, Zhikai; Wang, Haitao
CORPORATE SOURCE: Institute of Microbiology and Epidemiology, Academy of Military Medical Sciences, Beijing, 100071, Peop. Rep. China
SOURCE: Junshi Yixue Kexueyuan Yuankan (2002), 26(3), 176-178, 181
CODEN: JYKYEL; ISSN: 1000-5501
PUBLISHER: Junshi Yixue Kexueyuan Yuankan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The CHO expression system for the whole human anti-hepatitis A virus (anti-HAV) antibody was developed. The **light chain**

(VL-CL) of anti-HAV and its signal sequence were linked, then cloned into a mammalian expression vector, pCI-nec. The **heavy chain** signal sequence, the variable region, the first constant region(VH-Cm) and Fc fragment sequence were ligated to form a full length **heavy chain** ORE, which was then cloned into another mammalian expression vector, pCdhfrl. CHO/**dhfr cells** were cotransfected with the light and **heavy chain** expression vectors, and **cell** clones expressing human anti-HAV antibodies were selected by G418 and methotrexate (MTX). The recombinant human antibodies were purified with **protein** L affinity chromatog. from the **cell** culture medium. ELISA revealed that anti-HAV antibodies were expressed in culture medium. In reducing SDS-PAGE, the recombinant IgG exhibited two bands of approx. 50000 and 25000, resp. Western-blot demonstrated that both the whole IgG without reductant and the **heavy chain** with reductant reacted with goat anti-human Fc antiserum. Whole human anti-HAY **antibody** was expressed in CHO **cells**, which provides the basis for genetically engineered **production** of **antibody** with complete function.

L20 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 22 Aug 2003
ACCESSION NUMBER: 2003:656883 HCAPLUS
DOCUMENT NUMBER: 139:196281
TITLE: Fusion **proteins** comprising humanized anti-G250 antigen antibody and tumor necrosis factor fragment for therapeutic use
INVENTOR(S): Renner, Christoph; Scott, Andrew
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068924	A2	20030821	WO 2003-US4243	20030212
WO 2003068924	A3	20041229		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004053365	A1	20040318	US 2003-365123	20030212
EP 1507859	A2	20050223	EP 2003-711002	20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-355838P P 20020213
WO 2003-US4243 W 20030212

AB Chimeric antibodies, as well as fusion **proteins** which comprise chimeric or humanized antibodies, are disclosed. The antibodies are humanized murine antibodies specifically bind to GM-CSF, CD30, and G250 antigen. The fusion **proteins** include biol. active portions of tumor necrosis factor, or full length tumor necrosis factor. Expression vectors adapted for **production** of the **antibodies**, as well as methods for **manufacturing** these, are also disclosed.

IT **9002-03-3, Dihydrofolate reductase**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of chimeric **proteins** comprising humanized anti-GM-CSF antibody and tumor necrosis factor for therapeutic use)

L20 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 22 Aug 2003
ACCESSION NUMBER: 2003:656879 HCAPLUS
DOCUMENT NUMBER: 139:196280
TITLE: Preparation of chimeric **proteins** comprising humanized anti-GM-CSF antibody and tumor necrosis factor for therapeutic use
INVENTOR(S): Renner, Christoph; Scott, Andrew; Burgess, Antony
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068920	A2	20030821	WO 2003-US4185	20030212
WO 2003068920	C2	20040603		
WO 2003068920	A3	20040701		
WO 2003068920	C1	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004053365	A1	20040318	US 2003-365123	20030212
EP 1530580	A2	20050518	EP 2003-713430	20030212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-355838P P 20020213
WO 2003-US4185 W 20030212

AB Chimeric antibodies, as well as fusion **proteins** which comprise chimeric antibodies, are disclosed. The antibodies specifically bind to GM-CSF, CD30, and G250 antigen. The fusion

proteins include biol. active portions of tumor necrosis factor, or full length tumor necrosis factor. Expression vectors adapted for **production** of the **antibodies**, as well as methods for **manufacturing** these, are also disclosed.

L20 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 May 2003
ACCESSION NUMBER: 2003:376298 HCAPLUS
DOCUMENT NUMBER: 138:384248
TITLE: Recombinant **protein** production in human **cell** PER.C6 transformed with adenoviral E1 **protein** genes
INVENTOR(S): Bout, Abraham; Hateboer, Guus; Verhulst, Karina Cornelia; Uytdehaag, Alphonsus Gerardus; Schouten, Govert Johan
PATENT ASSIGNEE(S): Neth.
SOURCE: U.S. Pat. Appl. Publ., 61 pp., Division of U. S. Ser. No. 549,463.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003092160	A1	20030515	US 2002-234007		20020903
US 6855544	B1	20050215	US 2000-549463		20000414
US 2005170463	A1	20050804	US 2005-70890		20050302
PRIORITY APPLN. INFO.:			US 1999-129452P	P	19990415
			US 2000-549463	A3	20000414
			US 2002-234007	A2	20020903

AB Methods and compns. for the production of recombinant **proteins** in a human **cell** line. The methods and compns. are particularly useful for generating stable expression of human recombinant **proteins** of interest that are modified post-translationally, for example, by glycosylation. Such **proteins** may have advantageous properties in comparison with their counterparts produced in non-human systems such as Chinese hamster ovary **cells**. Thus, human **cell** line PER.C6 was transfected with plasmids containing the gene encoding the adenoviral transcription factor E2A and a variety of genes for **proteins** of interest.

IT **9002-03-3P, Tetrahydrofolate Dehydrogenase**
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(recombinant **protein** production in human **cell** PER.C6 transformed with adenoviral E1 **protein** genes)

L20 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 02 May 2003
ACCESSION NUMBER: 2003:334823 HCAPLUS
DOCUMENT NUMBER: 138:352761
TITLE: Anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening

INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schuelke, Norbert; Gardner, Jason; Ma, Dangshe
PATENT ASSIGNEE(S): PSMA Development Company, L.L.C., USA
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464239	AA	20030501	CA 2002-2464239	20021023
EP 1448588	A2	20040825	EP 2002-802198	20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005523683	T2	20050811	JP 2003-537481	20021023
US 2004033229	A1	20040219	US 2003-395894	20030321
US 2004161776	A1	20040819	US 2003-695667	20031027
US 2005215472	A1	20050929	US 2004-976352	20041027

PRIORITY APPLN. INFO.:

US 2001-335215P	P	20011023
US 2002-362747P	P	20020307
US 2002-412618P	P	20020920
WO 2002-US33944	W	20021023
US 2003-395894	A2	20030321
US 2003-695667	A2	20031027

AB The invention includes **antibodies** or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of PSMA, compns. containing one or a combination of such **antibodies** or **antibodies** or antigen-binding fragments thereof, hybridoma **cell** lines that **produce** the **antibodies**, and methods of using the **antibodies** or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA **proteins**, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST

(Analytical study); BIOL (Biological study); USES (Uses)
(anti-prostate specific membrane antigen (PSMA) antibodies and fragments for cancer diagnosis and therapy and antitumor screening)

L20 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 19 Sep 2002
ACCESSION NUMBER: 2002:709689 HCAPLUS
DOCUMENT NUMBER: 137:211928
TITLE: Construction of eukaryotic expression system and its uses for antibody cloning
INVENTOR(S): Yang, Zhihua; Ran, Yuliang
PATENT ASSIGNEE(S): Institute of Tumors, Tumor Hospital, Chinese Academy of Medical Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 31 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1328157	A	20011226	CN 2000-108065	20000609
PRIORITY APPLN. INFO.:			CN 2000-108065	20000609

AB The invention relates to construction of plasmid vector for expression of antibody in eukaryote. The vector contains selective marker gene (such as aminoglycoside phosphate transferase, thymidine kinase, hygromycin B phosphate transferase, xanthine-guanine phosphoribosyltransferase, or asparagine synthase) and extensible selective marker gene (such as dihydrofolic acid reductase (**dhfr**) or **glutamine synthase**). The vector also contains weak promotor (such as 72 bp fragment-deleted SV40) for driving the expression of the said marker genes. The vector also contains strong promotor (such as PhCMV-IE, PSV40-E, or PRSV-LTR) for driving the expression of antibody gene. The vector also contains enhancer sequence (such as 5'-non-translational region SP163 of mouse vascular endothelial growth factor). The vector further contains strong translation terminator (such as BGH polyA or SV40 polyA). The eukaryotic expression system is constructed by successively preparing general cloning vectors (such as pYR-GCVH and pYR-GCVL) of variable region of antibody, intermediate expression vectors (such as pYR-SV2-rdhfr and pYR-SV2-rneo) of antibody, and general eukaryotic expression vector (such as pYR-GSEVH, pYR-GSEVL, pYR-GCEVH, and pYR-GCEVL). The eukaryotic expression system is used to preparation and **production** of **antibodies** (such as chimeric **antibody**, modified **antibody**, humanized **antibody**, small mol. **antibody**, intracellular **antibody**, double-specific **antibody**, and other derivs.). The chimeric antibody of human VEGF and small mol. antibody of human carcino-embryonic antigen (CEA) were prepared by using the eukaryotic expression system in CHO-**dhfr**- **cell**.

IT **9023-70-5, Glutamine synthase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective marker gene **GS** in vector from; construction of eukaryotic expression system and its uses for antibody cloning)

IT **9002-03-3,** Dihydrofolic acid reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(selective marker gene **dhfr** in vector from; construction of eukaryotic expression system and its uses for antibody cloning)

L20 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 May 2002
ACCESSION NUMBER: 2002:354214 HCAPLUS
DOCUMENT NUMBER: 136:324066
TITLE: Humanized antibody to surface antigen pre-S2 of hepatitis B virus, and preparation process thereof
INVENTOR(S): Park, Seong Seop; Huh, Hyang Suk; Hong, Hyo Jeong
PATENT ASSIGNEE(S): Korea Green Cross Corporation, S. Korea; Korea Institute of Science and Technology
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2000055980	A	20000915	KR 1999-4939	19990212
PRIORITY APPLN. INFO.:			KR 1999-4939	19990212

AB A humanized antibody to surface antigen pre-S2 of hepatitis B virus (HBV) is provided, which maintains similar antigen-binding abilities with existing humanized antibody, but diminishes immune-causing abilities than existing humanized antibody obviously, so which can be used to prevent HBV infection and to treat the chronic hepatitis B. A process for the preparation of humanized **antibody** to HBV surface antigen pre-S2 comprises of: preparing humanized heavy-chained genes; preparing humanized light-chained genes; preparing representing vector (pCMV-HS2(II)**HC**) **producing** humanized **heavy -chain**; preparing representing vector (pKC-**dhfr** -HS2(II)) **producing** humanized **light-chain** ; culturing COS7 **cells**, and washing with OPTI MEM I; mixing pCMV-HS2(II)**HC**, pKC-**dhfr**-HS2(II) and Lipofectamine, adding OPTI MEM I, and pouring the mixture over the COS7 **cells**, culturing, concentrating, and measuring the concentration of the humanized **antibody** in COS7 **cell**; investigating binding ability of humanized **antibody** to HBV surface antigen pre-S2; and investigating binding affinity to antigen of humanized **antibody**.

L20 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 06 Oct 2000
ACCESSION NUMBER: 2000:707321 HCAPLUS
DOCUMENT NUMBER: 133:280571
TITLE: Process for **producing** monoclonal **antibody**
INVENTOR(S): Kusunoki, Chihiro; Fukushima, Atsushi
PATENT ASSIGNEE(S): Japan Tobacco Inc., Japan; Abgenix, Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058499	A1	20001005	WO 2000-JP2022	20000330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368734	AA	20001005	CA 2000-2368734	20000330
CA 2368734	C	20001005		
JP 2000342279	A2	20001212	JP 2000-97874	20000330
EP 1167537	A1	20020102	EP 2000-912975	20000330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 754808	B2	20021128	AU 2000-34563	20000330
PRIORITY APPLN. INFO.:			JP 1999-87929 A	19990330
			WO 2000-JP2022 W	20000330

AB Recombinant hybridomas are constructed by transferring a gene encoding an amino acid sequence, which is identical with the amino acid sequence of the **heavy chain polypeptide** of a specific monoclonal **antibody**, into immortalized B **cells** (hybridomas) **producing** this monoclonal **antibody**, thereby obtaining the monoclonal **antibody** in a significantly elevated amount from the liquid culture medium of the **cells**. Thus, transgenic mouse-**produced** human monoclonal anti-human interleukin 8 **antibody** was prepared and recombinant hybridoma K2.2.1 **producing** the anti-IL8 **antibody** was generated by introducing cDNA encoding secretory anti-human IL8 Ig. **heavy chain polypeptide**
.

IT **9002-03-3, Dihydrofolate reductase**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gene; process for **producing** monoclonal **antibody**
)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 06 Oct 2000
ACCESSION NUMBER: 2000:707212 HCAPLUS
DOCUMENT NUMBER: 133:280568
TITLE: Neutrokine-alpha binding **proteins** and methods based thereon
INVENTOR(S): Ruben, Steven M.; Ullrich, Stephen; Baker, Kevin
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
SOURCE: PCT Int. Appl., 398 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000058362	A1	20001005	WO 2000-US7966		20000324
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1577391	A1	20050921	EP 2005-12261		19961025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AU 2001054180	A5	20020725	AU 2001-54180		20010703
AU 779750	B2	20050210			
US 2002187526	A1	20021212	US 2002-84971		20020301
JP 2004129667	A2	20040430	JP 2003-362615		20031022
PRIORITY APPLN. INFO.:			US 1999-126599P	P	19990326
			US 2000-188208P	P	20000310
			AU 1996-76745	A3	19961025
			EP 1996-939612	A3	19961025
			JP 1998-520411	A3	19961025
			US 2000-533822	A1	20000324

AB The present invention relates to Neutrokine-alpha binding **polypeptides** (NAR). In particular, isolated nucleic acid mols. are provided encoding human NAR **protein.** NAR **polypeptides** are also provided as are vectors, host **cells** and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of NAR activity. The NAR **polypeptides, antibodies,** agonists and antagonists are useful for increasing B **cell** proliferation or Ig. **production,** and for treating immunodeficiencies and autoimmune diseases.

IT **9026-93-1, Adenosine deaminase**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(deficiency; neutrokine-α receptor/binding **proteins** and antibodies for treating immunodeficiency and autoimmune diseases)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 May 1998
ACCESSION NUMBER: 1998:273604 HCAPLUS
DOCUMENT NUMBER: 129:40190
TITLE: Comparison of the **production** of a human monoclonal **antibody** against HIV-1 by

heterohybridoma **cells** and recombinant CHO **cells**: A flow cytometric study

AUTHOR(S): Borth, Nicole; Strutzenberger, Karl; Donalies, Ute; Kunert, Renate; Katinger, Hermann

CORPORATE SOURCE: Institute for Applied Microbiology, University of Agriculture, Vienna, 1190, Austria

SOURCE: Cytotechnology (1996), 22(1-3), 129-138
CODEN: CYTOER; ISSN: 0920-9069

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **production** of human monoclonal **antibodies** for therapeutic use is of increasing importance for treatment of viral infections such as AIDS. As human x mouse heterohybridomas rarely reach the growth rates and **cell** specific production rates of mouse hybridomas, the transfection of standard **cell** lines, such as CHO or BHK, is a promising alternative. This has the addnl. advantage that the IgG subtype can be changed to suit the desired application. However, the use of a **cell** line that has not originally developed to **produce antibodies**, as lymphocytes and myeloma **cells** have, might have unrecognized drawbacks. This will be especially significant in the case of antibodies as each mol. consists of 4 chains linked by disulfide bonds which require specific intracellular factors to be properly folded and processed (**Heavy chain** binding **protein**, **Protein** Disulfide Isomerase a.o.). In this study, 2 **cell** lines were therefore compared: a human x mouse heterohybridoma **producing** IAM-2F5, a human IgG3 **antibody** specific for HIV-1 with neutralizing properties, and a Chinese Hamster Ovary **cell** transfected with **dihydrofolate reductase** and with the heavy and **light chain** genes of IAM-2F5 modified to IgG1. From each **cell** line 3 subclones were selected with low, medium, and high sp. production rates. Batch cultures were performed and the following cellular parameters analyzed by flow cytometry, 1) total RNA content (translational activity), 2) total **protein** content, 3) **cell** cycle phase distribution, 4) concentration of light and **heavy chains**, 5) concentration of helper **proteins** such as BiP and PDI. The production rate of heterohybridoma **cells** was best reflected in the intracellular concentration of kappa chain, while the gamma chain concentration was comparable for all 3 subclones. In the CHO **cells** the gamma chain expression and thus gene copy number appeared to be the limiting factor. The GRP78/BiP concentration in CHO remained unchanged in spite of a 5-fold higher concentration of gamma chain in the high producing subclone. The PDI concentration in CHO **cells** was much lower compared to the heterohybridoma **cells**, irresp. of production rates.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 16 May 1997

ACCESSION NUMBER: 1997:311170 HCAPLUS

DOCUMENT NUMBER: 126:304915

TITLE: A soluble derivative of a mammalian Fc receptor with pH-dependent binding of antibodies

INVENTOR(S): Gastinel, Louis N.; Bjorkman, Pamela J.

PATENT ASSIGNEE(S): California Institute of Technology, USA
SOURCE: U.S., 30 pp., Cont. of U. S. Ser. No. 819,413, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5623053	A	19970422	US 1993-4492	19930114
PRIORITY APPLN. INFO.:			US 1992-819413	B1 19920110

AB A soluble Fc receptor derivative (pHsFcR) that shows pH-regulated binding of antibodies is described. The receptor binds antibody in the pH range 5.5-6.5 and releases it in the pH range 7.5-8.5. This analog can still bind the β2-microglobulin **light chain** to form a fully functional receptor. In particular, the pH-sensitive Fc receptors of neonates are preferred. These derivs. have uses in e.g. the purification of **antibodies manufactured** on a large or small scale. The pHsFcR is a C-terminal truncation derivative lacking the transmembrane domain manufactured by expression of a cDNA for the receptor carrying in-frame stop codons. The pHsFcR is secreted into the growth medium upon expression of the cDNA in a suitable (prokaryotic or eukaryotic) host and can be purified from the medium by affinity chromatog. against an immobilized antibody. A truncation derivs. of the rat intestinal neonatal Fc receptor were prepared using sequence similarities with class I MHC antigens. Expression constructs for analogs carrying the phosphatidyl anchoring signal of decay-accelerating factor were constructed by standard methods. Bicistronic constructs carrying the gene for the β2-microglobulin **light chain** were also constructed. Manufacture of these analogs in CHO **cells** is demonstrated.

L20 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 14 May 1994
ACCESSION NUMBER: 1994:242521 HCAPLUS
DOCUMENT NUMBER: 120:242521
TITLE: Monoclonal and humanized antibodies to P-selectin and their therapeutic uses
INVENTOR(S): Chestnut, Robert W.; Polley, Margaret J.; Paulson, James C.
PATENT ASSIGNEE(S): Cytel Corp., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321956	A1	19931111	WO 1993-US4274	19930504

W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

EP 642356	A1	19950315	EP 1993-911098	19930504
EP 642356	B1	20030416		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, LU, MC, NL, SE				
JP 08503360	T2	19960416	JP 1993-519623	19930504
JP 3720352	B2	20051124		
NZ 286804	A	20000825	NZ 1993-286804	19930504
AT 237353	E	20030515	AT 1993-911098	19930504
ES 2197150	T3	20040101	ES 1993-911098	19930504
CA 2135083	C	20040106	CA 1993-2135083	19930504
US 5800815	A	19980901	US 1994-202047	19940225
WO 9425067	A1	19941110	WO 1994-US4935	19940504
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KG, KP, KR, KZ, LK, LU, LV				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				

PRIORITY APPLN. INFO.:	US 1992-880196	A2 19920505
	NZ 1993-252542	A1 19930504
	WO 1993-US4274	W 19930504
	IL 1993-105614	A 19930505
	US 1993-57292	B2 19930505
	US 1994-202047	A 19940225

AB The present invention relates to compns. and methods for treating inflammation and other pathol. conditions using novel blocking P-selectin antibodies which inhibit binding of an antibody secreted by a **cell** line designated ATCC Accession Number HB11041 to P-selectin as measured by a competitive inhibition assay. The antibodies of the invention may be used in the treatment of e.g. inflammatory and thrombotic diseases. **Production** of blocking and nonblocking monoclonal **antibodies** and humanized **antibodies** is described. The antibodies of the invention were tested in e.g. treatment of acute lung injury, myocardial ischemia and reperfusion, and leukocyte-endothelial **cell** interactions induced by degranulation of tissue mast **cells**.

L20 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 07 Aug 1993
ACCESSION NUMBER: 1993:447362 HCAPLUS
DOCUMENT NUMBER: 119:47362
TITLE: Disease-associated human autoantibodies specific for human thyroid peroxidase
INVENTOR(S): Rapoport, Basil
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9305072	A1	19930318	WO 1992-US7381	19920828
W: AU, CA, FI, JP, KR, NO, US				

	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
WO	9303146	A1	19930218	WO 1992-US6283	19920730
	W: AU, CA, FI, JP, KR, NO, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU	9225557	A1	19930405	AU 1992-25557	19920828
JP	07506960	T2	19950803	JP 1992-505362	19920828
EP	668918	A1	19950830	EP 1992-919338	19920828
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
FI	9400732	A	19940428	FI 1994-732	19940216
NO	9400668	A	19940429	NO 1994-668	19940225
PRIORITY APPLN. INFO.:				US 1991-750579 A2	19910828
				WO 1992-US6283 A	19920730
				US 1991-738040 A2	19910730
				WO 1992-US7381 A	19920828

AB Disease-associated human autoantibodies specific for human thyroid peroxidase (hTPO) are disclosed. Organ-specific anti-TPO human autoantibodies are disclosed which have been cloned, allowing definition of the autoantibody repertoire and the autoantigenic domains, encompassing a restricted immunodominant region on TPO recognized by patients with autoimmune thyroid disease. Compns. and diagnostic and therapeutic applications are also disclosed. Recombinant **production** of a secretable, truncated TPO is described, as are overprodn. of hTPO in nonthyroid eukaryotic **cells**, mol. determination of a B-**cell** epitope of TPO, determination of the role of TPO carbohydrate moieties in **antibody** recognition in Hashimoto's thyroiditis, cloning of genes for organ-specific anti-TPO human autoantibodies, etc.

IT **9002-03-3, Dihydrofolate reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(plasmid with genes for human thyroid peroxidase and, enhancement for production of human thyroid peroxidase in relation to)

FILE 'MEDLINE' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'BIOSIS' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'EMBASE' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'WPIDS' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'CONFSCI' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'SCISEARCH' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'JICST-EPLUS' ENTERED AT 17:01:20 ON 11 JAN 2006

FILE 'JAPIO' ENTERED AT 17:01:20 ON 11 JAN 2006

L21 30 S L20
L22 24 DUP REM L21 (6 DUPLICATES REMOVED)

L22 ANSWER 1 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-372382 [38] WPIDS
DOC. NO. CPI: C2005-115433
TITLE: New plasmid system comprises a first universal transfer vector, a second universal transfer vector, and an amplifiable vector, useful for expressing multi-subunit complex **proteins** including antibodies and receptors.
DERWENT CLASS: B04 D16
INVENTOR(S): SAHA, D P
PATENT ASSIGNEE(S): (SCHE) SCHERING CORP
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005047512	A2	20050526	(200538)*	EN	164

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2005176099	A1	20050811	(200553)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005047512	A2	WO 2004-US37721	20041110
US 2005176099	A1 Provisional	US 2003-519230P	20031112
		US 2004-986498	20041110

PRIORITY APPLN. INFO: US 2003-519230P 20031112; US 2004-986498 20041110
AN 2005-372382 [38] WPIDS
AB WO2005047512 A UPAB: 20050616
NOVELTY - A plasmid system (I) comprising in separate containers, a first universal transfer vector, a second universal transfer vector, and an amplifiable vector, is new.

DETAILED DESCRIPTION - A plasmid system comprising in separate containers:

(a) a first universal transfer vector comprising a first multiple cloning site and a nucleotide sequence comprising fully defined 2935 base pair (bp) sequence (SEQ ID NO. 2) given in the specification, where the first multiple cloning site is Bss HII, Pme I, Sna B1, Hin dIII, Asp 718, Kpn I, Pae R71, Xho I, Sal I, Acc I, Hinc II, Cla I, Eco RV, Eco RI, Pst I, Eco O1091, Apa I, Xma I, Bsp EI, Bam H1, Dsa I, Eag I, Ecl XI, Not I, Sac II, Xma III, Xba I, Sac I, Mlu I, Bcl I, Bsr GI, or Bss HII;

(b) a second universal transfer vector comprising a second multiple cloning site and a nucleotide sequence comprising fully defined 2941 bp sequence (SEQ ID NO. 1) given in the specification,

where the second multiple cloning site is Bss HII, Sgr AI, Xma I, Rsr II, Spe I, Sna B1, Hin dIII, Asp 718, Kpn I, Pae R71, Xho I, Sal I, Acc I, Hinc II, Cia I, Eco RV, Eco RI, Pst I, Eco O1091, Apa I, Xma I, Bsp EI, Bam H1, Dsa I, Eag I, Ecl XI, Not I, Sac II, Xma III, Xba I, Sac I, Nde I, Msc II, Nru I, Pac I, or Bss HII; and

(c) an amplifiable vector comprising a third multiple cloning site and a nucleotide sequence comprising fully defined 5144 bp sequence (SEQ ID NO. 3) given in the specification, where the third multiple cloning site is Sgr AI, Srf I, Xma I, Spe I, Sac II, Rsr II, Pac I, Nru I, Not I, Nde I, Msc I, Mlu I, Kpn I, Fse 1, Bss HII, Bsr GI, Bsp EI, Bcl I, Bbv C1, Pme I, Bss HII, Asc I, or Xba I.

INDEPENDENT CLAIMS are also included for:

(1) producing a **protein** (M1) comprising two or more types of **polypeptide**;

(2) **producing** an anti-IGFR1 **antibody** (M2);

(3) a kit comprising the plasmid system and one or more components selected from sterile, distilled water; calcium phosphate transformation reagents CaCl2 and 2X HEPES buffered saline; DEAE-dextran transformation reagents chloroquine in Phosphate buffered saline and phosphate buffered saline; DOTAP/cholesterol extruded liposomes; Transformation competent Escherichia coli; Dulbecco/Vogt modified Eagle's minimal essential medium (DMEM); Fetal calf serum; luria broth media; or paper instructions for usage of the plasmid system;

(4) an oligonucleotide primer comprising a nucleotide sequence selected from 3 fully defined 155, 160, or 166 base pair (bp) sequences (SEQ ID NO. 10, 11, or 12) given in the specification; and

(5) a plasmid comprising a nucleotide sequence selected from 4 fully defined 11520-13079 bp sequences (SEQ ID NO. 6-9) given in the specification.

USE - The plasmid system is useful for expressing multi-subunit complex **proteins** including antibodies and receptors (claimed). The plasmid system is used for recombinant **protein** expression in any **cell**, including mammalian **cell**, bacterial **cell**, yeast **cell**, or insect **cell**

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Dwg.0/16

L22 ANSWER 2 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-322962 [33] WPIDS

DOC. NO. CPI: C2005-100779

TITLE: New chromatin insulator, useful in expressing a gene of interest, in simultaneously expressing two or more genes or DNAs of interest or in the manufacture of a medicament for DNA-based therapy.

DERWENT CLASS: B04 D16

INVENTOR(S): CHATELLARD, P; IMHOF, M

PATENT ASSIGNEE(S): (ISTF) ARS APPLIED RES SYSTEMS HOLDING NV

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005040384	A1	20050506	(200533)*	EN	30

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP

KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA
NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR
TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005040384	A1	WO 2004-EP52591	20041020

PRIORITY APPLN. INFO: EP 2003-103890 20031021
AN 2005-322962 [33] WPIDS
AB WO2005040384 A UPAB: 20050524
NOVELTY - A new chromatin insulator comprising a sequence having 146 bp (SEQ ID Number 1), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a vector comprising one or more insulators;
(2) a host **cell** comprising the insulator or transfected with the vector; and
(3) producing a **polypeptide** of interest.
ACTIVITY - None given.
MECHANISM OF ACTION - Gene Therapy.
USE - The vector is useful in expressing a gene of interest, in simultaneous expression of two or more genes or DNAs of interest or in the manufacture of a medicament for DNA-based therapy (claimed).
Dwg.0/5

L22 ANSWER 3 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-092088 [10] WPIDS
DOC. NO. CPI: C2005-031170
TITLE: New nucleic acid molecule having a gene of interest, a scaffold/matrix attached region one an origin of replication, and a replication initiation factor, useful for expressing recombinant **proteins**.
DERWENT CLASS: B04 D16
INVENTOR(S): IVANOVA, L; SAUDAN, P
PATENT ASSIGNEE(S): (CYTO-N) CYTOS BIOTECHNOLOGY AG
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005005644	A1	20050120	(200510)*	EN	105

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2005064467 A1 20050324 (200526)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005005644	A1	WO 2004-EP7556	20040709

US 2005064467	A1	Provisional	US 2003-486238P	20030711
		Provisional	US 2003-524852P	20031126
			US 2004-888961	20040712

PRIORITY APPLN. INFO: US 2003-524852P 20031126; US 2003-486238P 20030711

AN 2005-092088 [10] WPIDS

AB WO2005005644 A UPAB: 20050211

NOVELTY - A nucleic acid molecule comprising at least one gene of interest, at least one scaffold/matrix attached region (S/MAR), at least one origin of replication (ORI), and at least one replication initiation factor capable of recognizing the at least one origin of replication, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an expression system comprising at least one nucleic acid molecule cited above, or at least one gene of interest, at least one S/MAR, at least one ORI, and at least one replication initiation factor capable of recognizing the at least one origin of replication;

(2) preparation of the nucleic acid molecule cited above, comprising inserting at least one S/MAR into a nucleic acid construct having at least one ORI, at least one gene of interest and at least one replication initiation factor;

(3) making a recombinant host **cell**, comprising introducing the nucleic acid molecule cited above or the expressions system of (1) into a host **cell**;

(4) a recombinant host **cell** produced by the method of (3), and comprising the nucleic acid molecule cited above, and/or at least one gene of interest, at least one S/MAR, at least one ORI, and at least one replication initiation factor capable of recognizing the at least one origin of replication;

(5) producing a **polypeptide** or untranslated RNA molecule, comprising introducing the nucleic acid molecule cited above or expression system of (1) into a host **cell** to produce a recombinant host **cell**, and culturing the **cell** for expression of the **polypeptide** or untranslated RNA molecule;

(6) a kit comprising the nucleic acid molecule cited above or the recombinant host **cell** of (4), or a transfection system selected from a lipid, polymer, **peptide** or porphyrin; and

(7) a kit for the production of a **polypeptide** or untranslated RNA molecule, comprising at least one nucleic acid molecule cited above or at least one recombinant host **cell** of (4).

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - The methods and compositions of the present invention are useful for the high level expression of **polypeptides** and/or untranslated RNA molecules, in particular for the rapid **production** of large quantities of recombinant **proteins** such as monoclonal **antibodies**, which can be used as drugs.

Dwg.0/3

L22 ANSWER 4 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-394969 [40] WPIDS

CROSS REFERENCE: 2003-845257 [78]

DOC. NO. CPI: C2005-122131

TITLE: Modulating an immune response for treating an immune dysfunction in a subject by administering a composition comprising a lymphocyte differentiation

factor.
DERWENT CLASS: B04
INVENTOR(S): MANN, P
PATENT ASSIGNEE(S): (MANN-I) MANN P
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005113299	A1	20050526	(200540)*		27

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005113299	A1 CIP of	US 2002-121481	20020410
	CIP of	WO 2003-US7019	20030306
		US 2004-941636	20040915

PRIORITY APPLN. INFO: US 2004-941636 20040915; US 2002-121481 20020410; WO 2003-US7019 20030306
AN 2005-394969 [40] WPIDS
CR 2003-845257 [78]
AB US2005113299 A UPAB: 20050624
NOVELTY - Modulating an immune response in a subject comprising administering to the subject a composition containing a lymphocyte differentiation factor sufficient to modulate the immune response, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) treating an immune dysfunction in a subject with or at risk of an immune dysfunction;

(2) reducing an inflammatory response in a subject with or at risk of an inflammatory response;

(3) treating inflammation in a subject with or at risk of inflammation;

(4) inhibiting tissue or **cell** damage in a subject caused by an inflammatory response or inflammation;

(5) treating existing tissue or **cell** damage in a subject caused by an inflammatory response or inflammation;

(6) treating splenomegaly in a subject;

(7) inhibiting proliferation or survival of a splenocyte in a subject having or at risk of having undesirable splenocyte proliferation or survival;

(8) stimulating differentiation or apoptosis of a splenocyte in a subject having or at risk of having undesirable splenocyte proliferation or apoptosis;

(9) reducing **antibody production** by a splenocyte in a subject having or at risk of having undesirable numbers of an **antibody**;

(10) reducing natural killer (NK) **cell** cytotoxicity in a subject having or at risk of having undesirable NK **cell** cytotoxicity;

(11) inhibiting rejection of a transplanted **cell**, tissue or organ in a subject;

(12) stimulating differentiation of lymphoid **cells**;

(13) a pharmaceutical composition comprising a unit dosage form

of PA sufficient to reduce an inflammatory response, inflammation in a subject; and

(14) a kit comprising a unit dosage form of PA to reduce an inflammatory response, inflammation or tissue or **cell** damage caused by an inflammatory response or inflammation in a subject, and instructions for use.

ACTIVITY - Antiinflammatory; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The method is useful in modulating an immune response for treating an immune dysfunction in a subject. The immune dysfunction comprises an autoimmune disorder. The autoimmune disorder comprises severe combined immunodeficiency (SCID), recombinase activating gene (RAG 1/2) deficiency, **adenosine deaminase** (ADA) deficiency, interleukin receptor chain deficiency, Janus-associated kinase 3 (JAK3) deficiency, reticular dysgenesis, primary T **cell** immunodeficiency, DiGeorge syndrome, Nude syndrome, T **cell** receptor deficiency, major histocompatibility complex (MHC) class II deficiency, TAP-2 deficiency (MHC class I deficiency), ZAP70 tyrosine kinase deficiency, purine nucleotide phosphorylase (PNP) deficiency, an **antibody** deficiency, X-linked agammaglobulinemia (Bruton's tyrosine kinase deficiency), autosomal recessive agammaglobulinemia, Mu **heavy chain** deficiency, surrogate **light chain** (5/14.1) deficiency, Hyper-IgM syndrome, X-linked (CD40 ligand deficiency), Ig **heavy chain** gene deletion, IgA deficiency, deficiency of IgG subclasses with and without IgA deficiency, common variable immunodeficiency (CVID), **antibody** deficiency with normal immunoglobulins, transient hypogammaglobulinemia of infancy, interferon receptor (IFNGR1 or IFNGR2) deficiency, interleukin 12 deficiency, interleukin 12 receptor deficiency, immunodeficiency with thymoma, Wiskott-Aldrich syndrome (WAS **protein** deficiency), ataxia telangiectasia (ATM deficiency), X-linked lymphoproliferative syndrome (SH2D1A/SAP deficiency) and hyper IgE syndrome. The inflammation is chronic or acute. The inflammation is at least in part **antibody** or **cell** mediated. The treatment results in a reduction in severity of a symptom of inflammation. The symptom comprises swelling, pain, headache, fever, nausea, skeletal joint stiffness, or tissue or **cell** damage. The treatment results in inhibition of **antibody production** or lymphoid **cell** proliferation. The tissue or **cell** damage is caused by a chronic or acute inflammatory response or inflammation. The inflammatory response or inflammation is at least in part **antibody** or **cell** mediated. The tissue or **cell** damage is present in thymus, liver, kidney, spleen, skin, or a skeletal joint. The skeletal joint comprises a knee, ankle, hip, shoulder, wrist, finger, toe or elbow. (All claimed.)

Dwg.0/1

L22 ANSWER 5 OF 24 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005262531 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15903249

TITLE: On the optimal ratio of heavy to **light chain** genes for efficient recombinant **antibody production** by CHO **cells**.

AUTHOR: Schlatter Stefan; Stansfield Scott H; Dinnis Diane M; Racher Andrew J; Birch John R; James David C

CORPORATE SOURCE: School of Engineering, University of Queensland, QLD

4072, Australia, and Lonza Biologics plc, 228 Bath Road, Slough SL1 4DX, UK.
SOURCE: Biotechnology progress, (2005 Jan-Feb) 21 (1) 122-33. Journal code: 8506292. ISSN: 8756-7938.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 20050521
Last Updated on STN: 20050708
Entered Medline: 20050707

AB Monoclonal antibodies (Mab) are heterotetramers consisting of an equimolar ratio of **heavy chain** (**HC**) and **light chain** (**LC**) **polypeptides**. Accordingly, most recombinant Mab expression systems utilize an equimolar ratio of **heavy chain** (**hc**) to **light chain** (**lc**) genes encoded on either one or two plasmids. However, there is no evidence to suggest that this gene ratio is optimal for stable or transient production of recombinant Mab. In this study we have determined the optimal ratio of **hc**:**lc** genes for production of a recombinant IgG4 Mab, cB72.3, by Chinese hamster ovary (CHO) **cells** using both empirical and mathematical modeling approaches. Polyethyleneimine-mediated transient expression of cB72.3 at varying ratios of **hc**:**lc** genes encoded on separate plasmids yielded an optimal Mab titer at a **hc**:**lc** gene ratio of 3:2; a conclusion confirmed by separate mathematical modeling of the Mab folding and assembly process using transient expression data. On the basis of this information, we hypothesized that utilization of **hc** genes at low **hc**:**lc** gene ratios is more efficient. To confirm this, cB72.3 Mab was transiently produced by CHO **cells** at constant **hc** and varying **lc** gene dose. Under these conditions, Mab yield was increased with a concomitant increase in **lc** gene dose. To determine if the above findings also apply to stably transfected CHO **cells** producing recombinant Mab, we compared the intra- and extracellular ratios of **HC** and **LC polypeptides** for three **GS**-CHO **cells** lines transfected with a 1:1 ratio of **hc**:**lc** genes and selected for stable expression of the same recombinant Mab, cB72.3. Intra- and extracellular **HC**:**LC polypeptide** ratios ranged from 1:2 to 1:5, less than that observed on transient expression of the same Mab in parental CHO **cells** using the same vector. In conclusion, our data suggest that the optimal ratio of **hc**:**lc** genes used for transient and stable expression of Mab differ. In the case of the latter, we infer that optimal Mab production by stably transfected **cells** represents a compromise between **HC** abundance limiting productivity and the requirement for excess **LC** to render Mab folding and assembly more efficient.

L22 ANSWER 6 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-758278 [74] WPIDS
DOC. NO. CPI: C2004-266126
TITLE: New immunogenic recombinant antibody comprising a part of a murine IgG2a subtype amino acid sequence and a mammalian glycosylation, useful in preparing a vaccine for immunizing primates against infectious or

autoimmune disorders.
DERWENT CLASS: B04 D16
INVENTOR(S): HIMMLER, G; LOIBNER, H; PUTZ, T; SCHUSTER, M; WAXENECKER, G
PATENT ASSIGNEE(S): (IGEN-N) IGENEON KREBS IMMUNTHERAPIE FORSCHUNGS
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004091655	A2	20041028	(200474)*	EN	59

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004091655	A2	WO 2004-EP4059	20040416

PRIORITY APPLN. INFO: AT 2003-599 20030417
AN 2004-758278 [74] WPIDS
AB WO2004091655 A UPAB: 20041117
NOVELTY - A new immunogenic recombinant antibody designed for immunization of primates comprises at least a part of a murine IgG2a subtype amino acid sequence and a mammalian glycosylation.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine comprising the antibody in a pharmaceutical formulation;

(2) a multicistronic **antibody** expression construct for **producing** an **antibody** in a Chinese Hamster Ovary (CHO) or HEK293 expression system, which contains at least a nucleotide sequence encoding a kappa **light chain** and a nucleotide sequence encoding a gamma **heavy chain**, where at least one of the nucleotide sequences encoding a kappa **light chain** or gamma **heavy chain** comprises a nucleotide sequence encoding at least a part of a murine IgG2a subtype amino acid sequence, and at least two IRES elements;

(3) a vector comprising a promoter, the antibody-expression construct and a transcription termination sequence;

(4) a CHO host **cell** or a HEK 293 transformed with the vector; and

(5) a method of **producing** an **antibody**.

ACTIVITY - Antimicrobial; Immunosuppressive.
No biological data given.
MECHANISM OF ACTION - Vaccine.
USE - The immunogenic recombinant antibody is useful in preparing a vaccine for immunizing primates against infectious or autoimmune disorders.
Dwg.0/10

L22 ANSWER 7 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-468875 [44] WPIDS
DOC. NO. CPI: C2004-175775
TITLE: Producing a **polypeptide** or untranslated RNA molecule comprises introducing at least one nucleic acid molecule into the at least one host **cell** to produce at least one recombinant host **cell**
.
DERWENT CLASS: B04 D16
INVENTOR(S): BACHMANN, M F; HENNECKE, F; SAUDAN, P; STERN, D M
PATENT ASSIGNEE(S): (CYTO-N) CYTOS BIOTECHNOLOGY AG
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004053137	A2	20040624	(200444)*	EN	63
RW:	AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW				
AU 2003283174	A1	20040630	(200472)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004053137	A2	WO 2003-CH810	20031210
AU 2003283174	A1	AU 2003-283174	20031210

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003283174	A1	Based on	WO 2004053137

PRIORITY APPLN. INFO: US 2002-432245P 20021211
AN 2004-468875 [44] WPIDS
AB WO2004053137 A UPAB: 20040712
NOVELTY - Producing a **polypeptide** or untranslated RNA molecule comprising introducing at least one nucleic acid molecule into the at least one host **cell** to produce at least one recombinant host **cell**, is new.
DETAILED DESCRIPTION - Producing a **polypeptide** or untranslated RNA molecule comprises:
(a) providing at least one host **cell**;
(b) introducing at least one nucleic acid molecule into the at least one host **cell** to produce at least one recombinant host **cell**, where the nucleic acid molecule comprises a first polynucleotide element capable of replicating the at least one nucleic acid molecule in said at least one host **cell**, and at least one second polynucleotide element selected from an open reading frame encoding a **polypeptide** of interest; a nucleotide sequence complementary to all or a part of the open reading frame of (i); and a nucleotide sequence encoding an untranslated RNA molecule or its

complement;
(c) selecting at least one stable recombinant host **cell** from the at least one host **cell**;
(d) culturing the at least one recombinant host **cell** under conditions suitable for expression of the **polypeptide** or untranslated RNA molecule; and
(e) controlling the reproducibility of the method for producing the **polypeptide** or the untranslated RNA molecule as a function of time.
An INDEPENDENT CLAIM is included for a method for producing a **polypeptide** or untranslated RNA molecule conforming to Good Manufacturing Practice (GMP), comprising carrying out the steps of the novel method.
USE - The methods are useful for producing a **polypeptide** or untranslated RNA molecule (claimed).
Dwg.0/5

L22 ANSWER 8 OF 24 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-419571 [39] WPIDS
DOC. NO. NON-CPI: N2004-333037
DOC. NO. CPI: C2004-157503
TITLE: New chimeric, humanized or CDR grafted antibody or its fragment capable of inhibiting human IL-6, useful for treating immune disorders, e.g. arthritis, inflammations, osteoporosis.
DERWENT CLASS: B04 D16 P13 P14
INVENTOR(S): GILES-KOMAR, J; KNIGHT, D; PERITT, D; TRIKHA, M; KNIGHT, D M; KOMAR, J G; MOHIT, T
PATENT ASSIGNEE(S): (CENZ) CENTOCOR INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004039826	A1	20040513	(200439)*	EN	117
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW					
BR 2002014168	A	20040914	(200469)		
AU 2002346369	A1	20040525	(200470)		
NO 2004002418	A	20040805	(200515)		
EP 1562968	A1	20050817	(200555)	EN	
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SK TR					
TW 2003001134	A	20030701	(200556)#		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004039826	A1	WO 2002-US36213	20021026
BR 2002014168	A	BR 2002-14168	20021026
		WO 2002-US36213	20021026
AU 2002346369	A1	AU 2002-346369	20021026
NO 2004002418	A	WO 2002-US36213	20021026

		NO 2004-2418	20040610
EP 1562968	A1	EP 2002-784436	20021026
		WO 2002-US36213	20021026
TW 2003001134	A	TW 2002-133208	20021113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
BR 2002014168	A Based on	WO 2004039826
AU 2002346369	A1 Based on	WO 2004039826
EP 1562968	A1 Based on	WO 2004039826

PRIORITY APPLN. INFO: WO 2002-US36213 20021026; US
2001-332437P 20011114; US
2001-332743P 20011114; TW
2002-133208 20021113

AN 2004-419571 [39] WPIDS

AB WO2004039826 A UPAB: 20040621

NOVELTY - A chimeric, humanized or CDR grafted antibody or its fragment capable of inhibiting human IL-6 comprising at least one heavy or **light chain** complementarity determining region (CDR) derived from the anti-IL-6 murine monoclonal antibody CLB-8 and a constant region derived from one or more human antibodies, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an isolated IL-6 antibody encoding nucleic acid;

(2) an isolated IL-6 antibody or its specified portion or variant comprising the antibody in (1);

(3) an IL-6 antibody encoding nucleic acid composition comprising the nucleic acid, and a carrier or diluent;

(4) an antibody vector comprising the nucleic acid;

(5) a host **cell** comprising the isolated nucleic acid;

(6) **producing** at least one IL-6 **antibody** or its specified portion or variant;

(7) an IL-6 antibody composition or specified portion or variant composition comprising the IL-6 antibody or specified portion or variant, and a carrier or diluent;

(8) treating an immune disorder or disease in a **cell**, tissue, organ or animal;

(9) modulating at least cancerous disorder or condition in a **cell**, tissue, organ or animal;

(10) a medical device comprising at least one of the antibody cited above;

(11) a formulation comprising at least one IL-6 antibody or specified portion or variant, and at least one selected from sterile water, sterile buffered water, or at least one preservative;

(12) treating at least one IL-6 mediated condition by administering the formulation to the patient;

(13) an article of **manufacture** for human pharmaceutical use comprising packaging material, and a container comprising a solution or a lyophilized form of at least one IL-6 **antibody** or its specified portion or variant;

(14) preparing the formulation; and

(15) a transgenic animal or plant expressing at least one of the antibody.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antirheumatic; Antiarthritic; Osteopathic.

No biological data given.